

New U.S. sites for STI trials

The clinical trial of the drug STI571 (or Gleevec as manufacturer Novartis has dubbed it) on patients with gastrointestinal stromal tumor (GIST) is being greatly expanded. From a Novartis-sponsored trial at three U.S. hospitals, a new National Cancer Institute-sponsored trial is at 15 U.S. cancer centers to date. Here they are:

California

Dr. Lee Rosen

Ph: 310-206-3170

Jonsson Comprehensive Cancer Center,
University of California, Los Angeles
<http://www.cancer.mednet.ucla.edu/>

District of Columbia

Dr. Dennis Pribat,

Ph: 202-877-2842

Washington Cancer Institute
Washington, D.C. 20010
<http://www.whcenter.org/>

Illinois

Dr. Christopher Ryan

Ph: 773-834-1676

University of Chicago Medical Center,
Chicago, Illinois
http://www.uchospitals.edu/index_js.html

Maryland

Dr. David Ettinger

Ph: 410-955-8846

Johns Hopkins Oncology Center

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List-serve etiquette:

To keep the Life Raft Group from being overwhelmed by the sheer number of messages, remember this tip: Send "attaboy" type replies *to the intended individual*, rather than the group as a whole. The sender's address can be found in the original message. E-mails that need to go to the whole group won't get buried in the deluge.

-- from Gary G.



BATTLING THE DRAGON

Initial survey shows high response rate

By Norman J. Scherzer
Life Raft Group Coordinator

This is our first attempt to look at the early reports from members about the effectiveness of STI571 against GIST. Janet Hendrickson and myself compiled the data and, although there is much work to be done, I wanted to provide a preliminary report as soon as possible.

Some caveats are in order. We are not professional researchers and the data collected about our experiences is subject to the twin demons of inaccuracy and distortion. Although we tried to be careful, we should be cognizant that patient-based reporting may not always be accurate. Also, there is no way of knowing how representative we are of the clinical trials as a whole. Finally, beware the pitfalls of small numbers. A small change can have a large statistical effect.

We must also be very careful not to dilute the research publications and presentations that are in the pipeline. The folks at Novartis and the clinical

researchers like Drs. George Demetri, Charles Blanke and Margaret von Mehren are entitled to the proper professional attention and respect due them.

Analysis: I included within the data all those who stayed on STI571 for all, or most, of the three-month clinical trial milestone. I excluded any who were off

Response of 16 Life Raft members at 3 months

	Number	Percent
No response — tumors grew	1	6.25%
Stable — no change	1	6.25%
25% or less shrinkage	0	0
25-50% shrinkage	6	37.5%
50% or more shrinkage	8	50%
Total response rate	14	87.5%

the drug for any substantial part of this period, even though they have arrived at the three-month milestone. There are two people in this category. I also excluded any person for whom we only

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The fast-track story of STI571

Robert Langreth and
Howard Banks
Forbes Magazine

At a frenetic factory outside the village of Ringaskiddy, Ireland, workers have spent the past year laboring in 12-hour shifts around the clock, seven days a week, turning out 10 tons of a plain-looking white powder with extraordinary

qualities.

The complex molecule is unusually difficult to synthesize. It started with 30 tons of raw materials and 500 tons of solvent. The process requires a dozen separate chemical steps and usually would take more than two years.

The factory has done it in half that

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New trial sites

From the front page

Baltimore, Maryland
<http://www.hopkinscancercenter.org/>

Massachusetts

Dr. George D. Demetri
Ph: 617-632-2200
Dana-Farber Cancer Institute
Boston, Massachusetts
<http://www.dana-farber.net/index.shtml>

Michigan

Dr. Laurence H. Baker
Ph: 734-647-8902
University of Michigan Comprehensive
Cancer Center
Ann Arbor, Michigan
<http://www.cancer.med.umich.edu/>

Minnesota

Dr. John Edmonson
Ph: 507-284-2511
Mayo Clinic Cancer Center
Rochester, MN
<http://www.mayo.edu/cancercenter/>

New York

Dr. Robert Maki
Ph: 212-639-5720
Memorial Sloan-Kettering Cancer Center,
New York, NY
<http://www.mskcc.org/>

Dr. Jerry Yates
Ph: 716-845-8547
Roswell Park Cancer Institute
Buffalo, NY, U.S.A.
<http://www.roswellpark.org/>

Dr. Karen H. Antman
Ph: 212-305-8602
Herbert Irving Comprehensive Cancer
Center, New York, NY
<http://cpmcnet.columbia.edu/dept/medicine/mesothelioma/irving.html>

Dr. Scott Wadler
Ph: 718-904-2754
Albert Einstein Comprehensive Cancer
Center, Bronx, NY
<http://www.aecom.yu.edu/cancer/default.htm>

Ohio

Dr. Ernest Borden

Ph: 216-444-8183
Cleveland Clinic Cancer Center
Cleveland, OH
<http://www.clevelandclinic.org/>

Oregon

Dr. Charles Blanke
Ph: 503-494-1267
Oregon Cancer Center at Oregon Health
Sciences University, Portland, OR
<http://www.ohsu.edu/occ/>

Pennsylvania

Dr. Margaret von Mehren
Ph: 215-728-3545
Fox Chase Cancer Center
Philadelphia, PA, U.S.A.
<http://www.fccc.edu/>

Texas

Dr. Robert Benjamin
Ph: 713-792-3626
M.D. Anderson Cancer Center
Houston, TX, U.S.A.
<http://www.mdanderson.org/>

— From CancerNet, a public service of the National Cancer Institute. Web address: <http://cancernet.nci.nih.gov/index.html>

Fast track

From the front page

time and is about to start the next huge batch.

There's good reason to rush: The white powder is an experimental drug called Glivec, and it may be the most potent weapon ever aimed at a common form of leukemia. Novartis is spending \$100 million on this 10-ton rush job, yielding enough powder to treat 30,000 patients for a year.

Daniel Vasella, chairman and chief executive of Novartis, is credited for putting the considerable weight of the huge drug company behind Glivec. He took that gamble somewhat brashly, after seeing astonishing early results in only 31 patients. Glivec was given to patients who weren't helped by existing therapy or couldn't tolerate it; remarkably, the new drug worked in all of them.

With patients clamoring for the drug, he told managers to ignore costs and crank up production fast. Clinical trials executives met with factory managers to explain the task's urgency.

Taking a huge risk as additional trials ensued, Novartis boosted production a

hundredfold, going from making merely kilograms to producing metric tons.

"If it didn't work, we'd have had to go back to square zero," says Andreas Rummelt, Novartis' manufacturing chief.

The typical drug takes five years or more of clinical testing to win regulatory approval. Novartis hopes to apply for approval in March, barely two and a half years after trials began. It would be one of the fastest tracks any drug has ever taken.

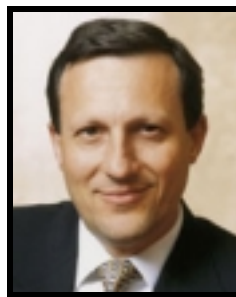
"The pace this has gone is nothing short of spectacular," says Oregon Health Sciences University oncologist Dr. Brian Druker, who led the first trial.

In current trials the drug is going to people with a less advanced form of the disease, too. It is testing the new drug against gastrointestinal stromal tumors, lung cancer and prostate cancer, as well. Novartis now has 3,500 patients trying Glivec. Some patients may be cured.

Such blazing speed is testimony to the big changes that Chairman and Chief Executive Daniel Vasella has put in

place at Novartis. Born in Fribourg, Switzerland, Vasella had experience with medicine all too early. When he was 8, he had tuberculosis and spent a year convalescing in an Alpine sanatorium. When he was 13 his father died of complications from routine surgery. An older sister died of lymphoma, and his other sister died in a car crash. Vasella grew up to become a doctor, taking a hospital post in Bern, but by his mid-30s he was restless.

Vasella came to realize that he enjoyed his management responsibilities more than his medical duties. When Sandoz, the big Swiss pharmaceutical outfit, offered him a job as a technical salesperson, he grabbed it.



Dr. Daniel Vasella, chairman and CEO of Novartis.

Who's new

Welcome to all new members of the Life Raft Group. Apologies to any of you who were left out, but this month's news-gathering by yours truly was interrupted by a trip to OHSU to start the trial!

— *Richard Palmer,*
newsletter editor

Dennis B.
Donald M.
Andrea F.
Mary Lou C.
(for brother Bob)

William M.
Bernie K.
Arthur B.
Chuck K.

Michael J.
(for wife Elsie)

Jocelyn K.
(for husband Donald)

James P.

GIST patient, on way to appointment



Yep, you read the headline right ... Mia Byrne took this photo in mid-January of husband Michael, a seven-year GIST survivor, on the slopes of Mount Hood in northern Oregon. The Byrnes couldn't resist getting in a little skiing as long as they were passing by, on their way to Michael's check-up at Oregon Health Sciences University in Portland. Offered as proof there IS life with cancer!

More fast track

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"I loved medicine, helping patients and working in a team. But I was also fascinated by business and wanted to try something new," he explains.

He joined Sandoz in 1987. Eight years later he was chief executive officer. A meteoric rise, even by U.S. standards.

Vasella helped create Novartis in the 1996, merging Sandoz with another huge Swiss company, Ciba-Geigy. He even suggested the new company's name; *novae artis* in Latin means "new skills."

Working quietly but urgently, Vasella has injected a distinctly American style of capitalism into Novartis. He expanded the bonus pool, created a stock-option plan and goaded Swiss unions into accepting performance-based incentives even for entry-level workers. Vasella also replaced complacent managers (15 of the top 21 posts turned over) and cut 12,500 jobs in two years, lifting the operating profit margin five points to 24 percent.

Today, Novartis has 10 other drugs in

human trials involving cancers of the breast, colon, brain, ovaries and pancreas. In the next two years Novartis will unleash a flood of new drugs for an array of other deadly or debilitating illnesses—asthma, diabetes, schizophrenia, organ failure, arthritis, skin disorders and eye disease.

It's enough, Vasella vows, to produce double-digit growth in coming years. "We have 24 drugs in late stages of testing," he says. "By all standards it is an extraordinarily high number."

Yet Vasella is still very much at home in the science of medicine. In 1999, the Wall Street Journal reported that Vasella spends evenings poring over research reports and meeting summaries, and he peppers his scientists with e-mails. He once caused the entire company network to crash because he copied too many people on a single file.

— *Editor's note: A much longer version of this story is available on Forbes' Web site, <http://www.forbes.com/forbes/2001/0205/022.html>*

Amazing ACOR spans the globe

Editor's note: The power of e-mail and the Internet, and the way they empower cancer patients was noted by Life Raft Group Coordinator Norman Scherzer. Here's an excerpt from a recent e-mail:

'Frankly, what is most amazing about this day was a dialogue between the son of a GIST patient in Japan and the son-in-law of a GIST patient in Israel helping to refer the latter to an STI571 site in Belgium — and all of this taking place on a server in the New York City apartment of Gilles Frydman, the president of ACOR ...'

**THE LIFE RAFT GROUP
BATTLING THE DRAGON WITH
GLIVEC (STI571)**

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The Life Raft Group

Who are we and what do we do? We are a group of patients and caregivers (spouses and others) in the STI571 (Glivec) GIST trials who have come together to share our experiences and support each other. Persons not in the trial are encouraged to seek support from the broader LMS community. We try to emphasize side effects, symptoms, and other drug-related issues. Members are encouraged to correspond privately to each other or to the wider group as appropriate to the specific issue.

Privacy: Privacy is of paramount concern. We respect the privacy of members, and promise not to send information that might be considered private to anyone outside of the group. We try to err on the side of privacy. To assist in that goal, we don't include professional members of the various study sites. However, this newsletter does serve as an outreach and receives widespread distribution. Hence, all items in the newsletter are edited to maintain the anonymity of members, except when those members have granted

publication of more detailed information.

Method: Our primary means of communication is through an e-mail group maintained by each member on their own computer. Occasional updates of general interest are provided to all members.

Disclaimer: We are patients and caregivers, not doctors. Any information shared among the group should be used with caution, and is not a substitute for careful discussion with your doctor.

Newsletter note: Read at your own risk! Every effort to achieve accuracy is made, but we are human and errors occur. Please advise the newsletter editor of any errors you may find.

Initial results

From Page 1

had a descriptive report (e.g. "responded" or "tumor shrinkage") rather than a specific percentage of tumor shrinkage. There were three in this category. Had I included this later group, the overall response rate to the drug would have been slightly higher.

The focus of this analysis was on the effectiveness of STI571 against GIST. In the future we will try to take a

more careful look at side effects, but there was not sufficient time, nor concise information, to do that in this article.

Let's take a look at the three-month group. It includes 16 Life Raft Member Patients, all in the Phase II clinical trial. Response is based solely upon CT scan reports regarding tumor changes. PET scan results were not included as they are not used universally at all sites, and as they may still be considered experimental tests.

Want the newsletter sent via e-mail?

It comes as a PDF (portable document format) file attachment. You'll need the free Adobe Acrobat Reader installed on your computer. It's very useful since many things on the Internet are PDF files. You'll find it at www.adobe.com/products/acrobat/readstep.html Just click "get Acrobat Reader free" and follow the steps; it's easy. To add your name to the e-mail mailing list, e-mail the editor at linda@interpac.net

Letters to the editor

Congratulations and a clarification

My brother just sent me a copy of the January Life Raft Group newsletter.

That's great! It's really helpful, especially if people don't have ready access to the web page.

Peter Rowbotham wrote that "One of the few concerns at this stage, is the potential for the development of resistance to STI. ... The commonest form of resistance in the research work seems to be an over-expression of the bcr-abl gene,



which I think means something like the bcr-abl protein ... has become ... bigger and stronger, so that normal doses of STI don't work any more. ..."

That's not "exactly" accurate.

Over-expression, here, would simply mean that the cells are producing larger amounts of the protein target (that is, bcr-abl in CML; c-kit in GIST). It does not necessarily mean that the protein itself is "bigger and stronger".

In other words, a common mechanism of drug resistance is simply that cells produce more of the normal target protein. This is what is commonly seen with

methotrexate, for example (see Medline reference *Guo et al., Mechanisms of methotrexate resistance in osteosarcoma, Clin Cancer Res 1999 Mar;5[3]:621-7*).

I have no idea whether this has been or will be observed with Glivec. Obviously, one hopes not!

Best regards,

Dr. David Josephy, professor
Dept. of Chemistry & BioChemistry
University of Guelph
Guelph, Ontario, Canada.

— Editor's note: Dr. Josephy's sister-in-law recently began the STI trial at Columbia Presbyterian.