Clinical Trial update for advanced resistant GIST

By Jim Hughes
LRG Clinical Trials Coordinator

There are several types of trials available for GIST patients including: treatment, adjuvant, observational, registry, continuation and post-marketing. This issue, we focus on the options for therapeutic treatment trials that are specifically for advanced resistant GIST.

Historically there has been one phase 3 or registration trial for advanced and resistant GIST every three years since Gleevec (imatinib) in 2001:

• 2000-2001/Gleevec - Approved for GIST on February 1, 2002. Registration trial was phase 2
• 2004/Sutent - Approved for GIST on January 26, 2006
• 2007/Tasigna - Phase 3 trial has stopped recruiting but is still collecting data. Tasigna is still not approved for GIST

In April 2009, a phase 3 registration trial of IPI-504 for resistant GIST was terminated following a higher than anticipated mortality rate among patients enrolled in the treatment arm.

USA and International:
1. Phase 3 Nilotinib Versus Imatinib (NCT00785785): This trial has 43 sites now recruiting. These include 15 sites in eight states in the US and 28 international sites in Austria, Canada, France, Japan, The Netherlands, Spain and Thailand.
2. Phase 3 Nilotinib plus Imatinib (NCT00751036): This trial is now re-

See UPDATE Page 2

It’s time to consider mutational status for resistant GIST patients

By Jerry Call
LRG Science Coordinator

This is the first article in a series discussing mutational status and resistant GIST. In this issue, we will begin with a brief overview and wild-type GIST.

In the not too distant future, we may have newer KIT inhibitors that overcome most types of GIST resistance. But for the present, it is becoming increasingly clear that GIST can be divided into four main types based on mutational status; KIT exon 11, KIT exon 9, PDGFRA D842V and wild-type GIST. In addition, there is another group comprising the “rare” mutations (KIT exons 13 & 17, etc). The different types have different initial responses to Gleevec and resistance occurs via somewhat different mechanisms. GIST patients and doctors can use this knowledge to their advantage in choosing a clinical trial or, in some cases, to consider off-label treatment options.

Clinical Trials

The GIST clinical trial era began in earnest in 2000 with the first Gleevec trials. For almost ten years now, almost all GIST trials have been inclusive trials allowing most or all of the various sub-types of GIST. Today, some clinical trials have broad inclusion criteria designed to “cast a wide patient net”. The intention has been if a diverse population of patients is exposed to a drug, that in addition to a group that is expected to respond, unexpected benefit might be seen in a population that was not predicted. While this approach has the potential to find unexpected benefit, it also has a downside, especially in registration trials. The downside is that the trial may not show enough overall benefit to be considered successful.

Conversely, a trial can be designed with more rigid criteria in an attempt to “enrich” the patient population. The goal would be to enroll only patients that are predicted to respond. An example of this is a new trial being planned by the National...
Institutes of Health (NIH). This trial will test a new class of drug called an IGF-1R inhibitor. The trial will only be for wild-type GIST patients (patients whose tumors have no mutation in the KIT or PDGFRA genes). While details are lacking, we expect this trial to allow both pediatric (under 18) and adult patients who have wild-type GIST. Preliminary information leads us to believe this trial will be for R1507, an IGF-1R inhibitor made by Roche.

The reason that the NIH is planning to limit the R1507 trial to patients with wild-type GIST is that the biology of wild-type is distinct from other types of GIST, and R1507 targets one of the differences. Several different research groups (Dr. Antonescu’s lab at Memorial Sloan-Kettering Institute, Dr. Godwin’s lab at Fox Chase Cancer Center, Dr. Corless’ lab at Oregon Health & Science University (OHSU)) have shown that IGF-1R is over-expressed in wild-type GIST. Most recently, Dr. Christopher Corless and colleagues at OHSU have shown that IGF-1R is over-expressed in two-thirds of patients with wild-type GIST. While IGR1R may be less important for other types of GIST, this is still under investigation.

The new IGF-1R inhibitor trial by the NIH is the most obvious example of a GIST trial where mutational status would be used to decide which patient might benefit the most from the trial. In fact, checking mutational status will be mandatory to ensure that the patients enrolled have wild-type GIST. Specifically targeted trials have a better chance of both answering the scientific question and benefiting the targeted patient population. The time has also come when patients with other mutational types might also have more potential to benefit from one type of trial compared to another type. Certain trials/sponsors might also stand to benefit from more selective trials. GIST can be broken down in many ways including by primary mutational status. When considering primary mutational status, GIST can be divided into four main types:

- KIT exon 11 mutations
- KIT exon 9 mutations
- PDGFRA exon 12 mutations
- PDGFRA exon 18, non D842V mutations

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Characteristics</th>
<th>Possible Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exon 11</td>
<td>• Secondary mutations are frequent</td>
<td>• Target KIT and secondary mutations</td>
</tr>
<tr>
<td>Exon 9</td>
<td>• Less sensitive to imatinib</td>
<td>• Higher dose IM or Sutent</td>
</tr>
<tr>
<td></td>
<td>• Less secondary mutations</td>
<td>• Much not known</td>
</tr>
<tr>
<td>PDGFRA</td>
<td>•Insensitive to imatinib</td>
<td>• D842V inhibitors</td>
</tr>
<tr>
<td></td>
<td>•Insensitive to sunitinib</td>
<td>• Dasatinib</td>
</tr>
<tr>
<td></td>
<td>• Primary resistance</td>
<td>• HSPI90 inhibitors</td>
</tr>
<tr>
<td>Wild-Type</td>
<td>• Imapitinib is a poor WT-KIT inhibitor</td>
<td>• Potent WT KIT inhibitors</td>
</tr>
<tr>
<td></td>
<td>•KIT may remain activated</td>
<td>• IGF-1R</td>
</tr>
<tr>
<td></td>
<td>• 2/3 overexpress IGF1R</td>
<td>• SDH?</td>
</tr>
<tr>
<td>Rare Mutations</td>
<td>• KIT exon 13</td>
<td>• Little clinical data</td>
</tr>
<tr>
<td></td>
<td>• KIT exon 17</td>
<td>• Some in-vitro data</td>
</tr>
<tr>
<td></td>
<td>• PDGFRA exon 12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PDGFRA exon 18, non D842V</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1

An independent investigation of genotype coupled with this trial had received no tumor samples to analyze.

5. Phase 1 BIIB028 (NCT 00725933): Dr. Jonathan Trent at MD Anderson (MDA) sent out a notice regarding a phase 1 trial in advanced solid tumors of HSP90 inhibitor BIIB028 that will accept GIST patients. The Principal Investigator at MDA is Dr. David Hong, 713-563-5844, dshong@mdanderson.org. Prior treatment with HSP90 inhibitors is excluded. BIIB028 is administered by IV twice weekly. Trial sites are open at MDA in Houston and at Los Angeles and Encinitas CA. The overall trial contact is via the Manufacturer, Biogen Idec at: oncologyclinicaltrials@biogenidc.com

You can find the details on all these trials and others in the LRG GIST Clinical Trial Database at: http://www.liferaftergroup.org/treat_trials.html. Use the pre-defined search links or click the “Search Trials” button at the top of the Clinical Trials frame.

The Life Raft Group

Who are we, what do we do?

The Life Raft Group (LRG) directs research to find a cure for a rare cancer and help those affected through support and advocacy until we do. The LRG provides support, information and assistance to patients and families with Gastrointestinal Stromal Tumor (GIST). The LRG achieves this by providing an online community for patients and caregivers, supporting local in-person meetings, patient education through monthly newsletters and webcasts, one-on-one patient consultations, and most importantly, managing a major research project to find the cure for GIST.

Disclaimer

We are patients and caregivers, not doctors. Information shared is not a substitute for discussion with your doctor. For the very latest information, see the LRG Clinical Trials database at: http://liferaftergroup.org/treat_trials.html.
Wild-type GIST

The case that mutational testing can be useful for clinical trial decision-making is most apparent when looking at PDGFRA D842V mutations and wild-type GIST. These two groups are quite different from the KIT exon 11 and exon 9 groups, both in their initial response to drugs and in resistance. In this month’s issue of the LRG Clinical Trials Bulletin, we will discuss a rationale for decision-making for wild-type GIST. In upcoming editions of the Bulletin, we will discuss other mutational types.

Even though the KIT gene is not mutated in wild-type GIST, Dr. Katherine Janeway of Dana-Farber has shown that the KIT protein is still activated in wild-type, specifically in patients with the pediatric form of wild-type. In support of the importance of KIT signaling, we also know that some patients with wild-type have responded to chronic myelogenous leukemia (CML). There are many examples of drugs that appeared to work in the lab and failed in clinical trials (including examples in trials with GIST patients).

See Figure 1 for an overview of mutational types and possible strategies.

Table 1: Wild-type GIST

<table>
<thead>
<tr>
<th>Without SDH mutations</th>
<th>WITH SDH mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two treatment options</td>
<td>Could pursue a SDH directed path OR A WT-GIST path</td>
</tr>
</tbody>
</table>

Potent wild-type KIT inhibitors | IGF-1R inhibitors | SDH directed therapies
---|---|---
• Sutent<sup>1</sup> | • Many drugs in trials | • HIF1α inhibitors<sup>3</sup>
• Tasigna<sup>2</sup> | • Affects 2/3 of WT-GIST | • Derivatives of a ketoglutarate
• No secondary mutations | • No GIST specific trials | • Dichloroacetate (DCA)
• Little need for a “wide spectrum” KIT inhibitor | • Planned NIH trial | One phase I trial combines both: potent WT-KIT inhibitor (Sutent) + IGF-1R inhibitor (CP-751,871)

1. Approved for GIST.
2. Approved for CML, in trials for GIST
3. HIF1α inhibitors may be a more advanced concept than the other two SDH directed strategies. All of the SDH directed therapies probably have less evidentiary support than the therapies for wild-type GIST without SDH mutations.

ADVANCED
FROM PAGE 1

The options available today do not include any phase 3 or registration trials in GIST. As in much of the past, there is presently a mix of phase 1 and 2 trials of potential therapies and varying strategies.

United States

Sorafenib Phase 2: This trial, sponsored by the University of Chicago under Dr. Hedy Kindler, has been running for four years and is very near the accrual goal. Currently this trial is open in Chicago. However, several sites outside Chicago have recruited patients in the past. Interim results were reported at the 2008 American Society of Clinical Oncologists conference (ASCO). Out of 24 patients, three had partial response and 14 had stable disease as best response for a total 71 percent benefit rate. Because sorafenib controls a broad range of resistant GIST mutations there have been recent calls to evaluate sorafenib as second-line therapy in place of sunitinib. This phase 2 trial would be a good option for exon 11 patients failing both imatinib and sunitinib, but it will close shortly.

Nilotinib Phase 2: This trial is only at Fox Chase Cancer Center. It was initiated to provide an option to access nilotinib after closure of the phase 3 registration trial. It requires a weekly visit for the first month then every four weeks afterwards. Results from this trial and the phase 3 trial have yet to be reported. However, at ASCO 2008 there was a report on the patients in the nilotinib compassionate access program. These patients could not participate in the phase 3 trial and were resistant to both imatinib and sunitinib. Of the 42 patients evaluable, four achieved partial response and 15 had stable disease for a total 45 percent benefit rate.

Nilotinib probably has a lower level of side-effects compared to imatinib, sunitinib and sorafenib. For patients intolerant of standard therapies, nilotinib may be an alternative to moving directly to sorafenib. Nilotinib is also reported to have excellent activity against wild-type KIT. This trial would provide access for those unable to obtain nilotinib off-label. However, it re-

JERRY
FROM PAGE 2

• Wild-type GIST
• PDGFRA D842V mutations

In addition to the four main types, there are a number of rare mutations (less than 1% each) that can be lumped into another group for which there is little clinical data. In this group, in-vitro data can give some guidance. This group includes KIT exon 13, KIT exon 17, PDGFRA exons 12 and 13 and PDGFRA exon 18 mutations other than the D842V mutation.

At its most basic, matching a mutation type to a clinical trial requires knowing both the primary mutation status and potential effectiveness of the trial drugs against that mutation. Evidence of effectiveness typically comes from lab experiments although in some cases it can come from earlier clinical trials. Although lab evidence can suggest that one strategy might be more appropriate than another strategy, ultimately effectiveness must be proven in a clinical trial. There are many examples of drugs that appeared to work in the lab and failed in clinical trials (including examples in trials with GIST patients).

See Table 1: Wild-type GIST for an overview of mutational types and possible strategies.
Sutent and Gleevec are currently approved KIT inhibitors against wild-type KIT. Label treatment. Table 2 shows the potency of selected mutations and three main treatments in the SDH genes. This testing can be done to identify additional testing for mutation status. Dr. Lee Helman from the NIH, has been involved in the Mayo Clinic and Dr. Constanine Stratakis, Dr. Su Young Kim and Dr. Lee Helman from the NIH, have shown that a subset of wild-type GISTs have mutations in one of four genes that form the SDH complex.

So the first step for wild-type patients might be to do additional testing for mutations in the SDH genes. This testing can be done by the NIH (contact Dr. Su Young Kim for details). With complete mutational testing that includes testing for SDH mutations, wild-type GIST can be sub-divided into two main mutation types and three main treatment categories as shown in Table 1.

Off-label treatment

In addition to clinical trials, some GIST patients may have the opportunity for off-label treatment. Table 2 shows the potency of approved KIT inhibitors against wild-type KIT. While these drugs are all approved, only Gleevec and Sutent are currently approved for GIST. The other drugs listed are all in clinical trials for GIST.

As can be seen from Table 2, Gleevec is not a very good inhibitor of wild-type GIST. In fact, Gleevec is about 10 times more potent at inhibiting KIT exon 11 mutations compared to wild-type KIT (data not shown here). For patients with wild-type GIST, Gleevec may not inhibit wild-type KIT strongly enough. This opens the possibility that these patients might respond better to a more potent wild-type KIT inhibitor.

Important points to remember about wild-type GIST:
- Resistance is not driven by secondary mutations
- KIT signaling still appears to be important
- The relative potency of a drug against wild-type KIT appears to be more important than the drugs ability to inhibit many different secondary mutations
- IGF-1R signaling may be important. IGF-1R is over-expressed in 2/3 of wild-type GIST and represents a new therapeutic target.
- Little is known about the best way to treat GISTs in patients with SDH mutations. One possibility may be to target SDH mechanisms rather than KIT, however this remains speculative.

As demonstrated by wild-type GIST, knowing the GIST mutation type offers new opportunities for more tailored targeted therapies. Next issue we will discuss the importance of other mutation types in the selection of therapy options.
against D842V. Patients with this mutation may want to consider this trial and possibly an HSP90 trial. The benefit of dasatinib for other secondary mutation types is not as clear. Like sunitinib, dasatinib inhibits a subset of the most frequent secondary mutations.

**SF1126 Phase 1:**  
SF1126 is a novel drug in GIST. It targets the PI3K protein which is in the downstream signal path of the KIT and PDGFRA oncoproteins. Therefore, primary and secondary KIT/PDGFRA mutation status may be less important. Early results reported at ASCO 2009 indicated stability in three GIST patients. SF1126 inhibits a broad range of PI3K/P110 isoforms, but it does not inhibit KIT or PDGFRA, although future trials may include combinations with KIT/PDGFR inhibitors. This will be an interesting strategy to watch develop. This trial would be suitable for patients who have failed both imatinib and sunitinib and require twice weekly site visits for intravenous (IV) infusions. Sites are open in Indianapolis, Atlanta, Scottsdale and Tucson.

**Doxorubicin + Flavopiridol Phase 1:**  
This trial has been ongoing since 2004. As of late last year, it had not accrued any GIST patients. Flavopiridol inhibits Cyclin-dependent kinase (CDK) which regulates the cell cycle. It also inhibits transcription of KIT. In the lab, Flavopiridol has been shown to cause GIST cell death. However, this trial also includes a chemotherapy agent (Doxorubicin) which has not been shown to be effective in GIST as a single agent. Both drugs are administered by IV and the trial requires site visits every three weeks.

**International**  
The options for advanced GIST patients experiencing resistance are even more limited on an international basis. GIST specific trials are few and sites are widespread.

**Imatinib versus Nilotinib Phase 3:**  
This trial is just getting underway in Latin America with the first site opening in Colombia, but additional sites are planned in Southeast Asia and Russia. Patients who are failing 400 mg imatinib are eligible. Patients who have used more than 400 mg of imatinib or other tyrosine kinase inhibitors are excluded. This trial is suitable for most patients who experience resistance at 400 mg of imatinib.

**Sunitinib Phase 4:**  
This trial in China is testing safety and efficacy in imatinib resistant patients. Patients who may be unable to access nilotinib under the current health authority may do so in this trial at three locations in Beijing and one in Nanjing.

**Nilotinib Phase 2:**  
This trial in Israel is testing the safety and efficacy of nilotinib in imatinib and sunitinib resistant patients. Patients who may be unable to access nilotinib under the current health authority may do so in this trial at sites in Tel Aviv and Tel Hashomer.

**Oral Angiogenesis Inhibitor Phase 4:**  
This trial is looking at the effect of antiangiogenesis therapy on tumor size and growth. It has sometimes been observed that tumors appear to grow on antiangiogenic drugs as a result of necrosis and edema caused by the positive effects of therapy. The inherent risk is that patients are being removed from treatment because of growth that is really an artifact. This trial looks at tumor growth patterns over a period of four weeks both during and after stopping anti-angiogenic therapy. Sunitinib is antiangiogenic through inhibition of VEGF. Both GIST and Renal Cell Cancer patients are eligible. This trial might be appropriate for patients who are on sunitinib and who would benefit from the additional monitoring (MRI and PET scans) that are part of the protocol. This trial is only open in Nijmegen, Netherlands.

**Everolimus Phase 2:**  
This trial at five sites in Germany is for patients failing both imatinib and sunitinib. Everolimus targets mTOR, a protein in the signal path downstream from KIT/PDGFR. In theory, this drug is appropriate for any GIST mutation type. An Italian poster at ASCO 2009 indicated everolimus combined with imatinib or PKC412 produced response in patients with PDGFRA mutation D842V. It is not
clear from the protocol of this trial if concurrent imatinib or sunitinib therapy is allowed with everolimus.

**Imatinib + IL-2 Phase 1:** This trial has been running since 2006. The goal at the outset was to enroll five GIST patients. The research behind this trial indicates that imatinib has an alternative mode of attacking GIST via the immune system. IL-2 is normally produced in the body during an immune response. Adding IL-2 to imatinib could enhance the immune response. This trial is appropriate for patients failing standard treatments. IL-2 is administered by IV during the second week of a three week cycle. This trial is currently open at Institute Gustave Roussy in Villejuif, France.

**Multi-Bacteria Vaccine (MBV) Phase 1:** In a 2008 paper in the International Journal of Cancer, researchers in Germany and Switzerland showed the association of high levels of NY-ESO-1 type antigens in GIST tumors with aggressive tumor behavior. NY-ESO-1 was expressed in 20 percent of the GISTS tested. MBV can take advantage of this marker and theoretically direct the body’s immune system to attack tumor cells expressing NY-ESO-1. Patients who either progress or are intolerant on imatinib and sunitinib are eligible. Patient tumor samples must also test positive for NY-ESO-1 type antigens in GIST tumors with aggressive tumor behavior. NY-ESO-1 was expressed in 20 percent of the GISTS tested. MBV can take advantage of this marker and theoretically direct the body’s immune system to attack tumor cells expressing NY-ESO-1. Patients who either progress or are intolerant on imatinib and sunitinib are eligible. Patient tumor samples must also test positive for NY-ESO-1 type antigens in GIST tumors with aggressive tumor behavior. NY-ESO-1 was expressed in 20 percent of the GISTS tested. MBV can take advantage of this marker and theoretically direct the body’s immune system to attack tumor cells expressing NY-ESO-1. Patients who either progress or are intolerant on imatinib and sunitinib are eligible. Patient tumor samples must also test positive for NY-ESO-1 type antigens in GIST tumors with aggressive tumor behavior. NY-ESO-1 was expressed in 20 percent of the GISTS tested. MBV can take advantage of this marker and theoretically direct the body’s immune system to attack tumor cells expressing NY-ESO-1. Patients who either progress or are intolerant on imatinib and sunitinib are eligible. Patient tumor samples must also test positive for NY-ESO-1 type antigens in GIST tumors with aggressive tumor behavior.

**Future trial directions for Advanced GIST**

We occasionally hear about clinical trial plans from well-placed sources who communicate unofficially. Here is the latest:

**LBH589 Phase 1 & 2 for GIST:** This trial is in the later planning stages in Europe. LBH589 is an HDAC inhibitor that can affect the transcription of the KIT gene. It can also act to inhibit HSP90. Trial plans include a phase 1 & 2 study combining imatinib and LBH589 for patients who have failed standard treatment. The trial is expected to come on-line by the end of this year.

**AUY922 for GIST:** Planning has started in the United States for a trial of AUY922. AUY922 is a very potent HSP90 inhibitor. A combination trial with imatinib is being considered; if a combination, this trial will probably start as a phase 1 in order to address dosage and safety issues.

**STA-9090 in GIST:** This drug has been in phase 1 trials for solid tumors since late 2007. It has been reported to be one of the most effective HSP90 inhibitors in the lab. One of the first trial sites was Dana Farber Cancer Institute which continues to be the focus of plans for a follow-up trial in GIST.

**SF1126 in GIST:** At ASCO 2009, Dr. Gabriela Chiorean at the University of Indiana in Indianapolis presented encouraging results of a phase 1 trial in solid tumors that included GIST patients. SF1126 is a PI3K inhibitor that can work against a variety of GIST mutations. Dr. Chiorean expressed interest in a follow-up phase 2 trial in GIST.

**Deciphera:** This start-up has a new approach to inhibiting KIT that does not depend on blocking the ATP binding pocket, as do the current generation drugs imatinib and sunitinib. The new design may block KIT irrespective of mutation type. We are looking for phase 1 trials to start in 2010 in GIST.

**R1507 for Wild Type GIST:** Plans seem to be underway at the National Institutes of Health for a phase 2 trial in wild type GIST. We have been hearing for some time that a trial is months away.
Note: Trials are first grouped together by treatment phase. For example, the first grouping lists 2 trials that are open to patients in all treatment stages. Each trial description also lists the treatment stage under the "Stage" heading. Trials that are specifically for GIST are listed first. Trials are then sorted by phase in descending order and then by drug name. Trial sites are sorted by country, state and then city.

<table>
<thead>
<tr>
<th>Treatment Stage:</th>
<th>All</th>
<th>First-line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td></td>
<td>Imatinib + Bevacizumab</td>
</tr>
<tr>
<td><strong>Imatinib Mesylate in Treating Patients With Liver Metastasis From a Gastrointestinal Stromal Tumor</strong></td>
<td></td>
<td><strong>Imatinib Mesylate With or Without Bevacizumab in Treating Patients With Metastatic or Unresectable Gastrointestinal Stromal Tumor</strong></td>
</tr>
<tr>
<td>Phase: 2</td>
<td>Phase: 3</td>
<td></td>
</tr>
<tr>
<td>Stage: All</td>
<td>Stage: First-line</td>
<td></td>
</tr>
<tr>
<td>Conditions: Gastrointestinal Stromal Tumor</td>
<td>Conditions: Gastrointestinal Stromal Tumor</td>
<td></td>
</tr>
<tr>
<td>Drug Type: KIT/PDGFRα inhibitor</td>
<td>Drug Type: KIT/PDGFRα inhibitor+VEGF inhibitor (antibody)</td>
<td></td>
</tr>
<tr>
<td>Strategy: Block KIT</td>
<td>Strategy: Block KIT</td>
<td></td>
</tr>
<tr>
<td>NCT #: NCT00764595</td>
<td>NCT #: NCT00324987</td>
<td></td>
</tr>
<tr>
<td>Contact: See site contact info below Niigata University Medical and Dental School Niigata, Japan 81-25-227-2228 Tatsuo Kanda, MD</td>
<td>Contact: See each trial site.</td>
<td></td>
</tr>
</tbody>
</table>

**Surgery**

**Surgery in Treating Patients With Liver Metastasis From a Gastrointestinal Stromal Tumor**

| Phase: 2 | Phase: 3 |
| Stage: All | Stage: First-line |
| Conditions: Gastrointestinal Stromal Tumor | Conditions: Gastrointestinal Stromal Tumor |
| Drug Type: Surgery | Drug Type: Surgery |
| Strategy: Surgery | Strategy: Surgery |
| NCT #: NCT00769782 | NCT #: NCT00324987 |
| Contact: See site contact info below Niigata University Medical and Dental School Niigata, Japan 81-25-227-2228 Tatsuo Kanda, MD | Contact: See each trial site. |

**Tom Baker Cancer Center**

Calgary, Alberta Canada
403-521-3707
Vivien H.C. Bramwell, MB, BS, PhD, FRCP

**USC/Norris Comprehensive Cancer Center**

Los Angeles, CA USA
Clinical Trials Office
323-865-0451

**Lombardi CCC at Georgetown University**

Washington, DC USA
Clinical Trials Office
202-444-0381

**Iowa Oncology Research Association - CCOP**

Des Moines, IA USA
515-244-7586
Robert J. Behrens, MD

**University of Chicago**

Chicago, IL USA
Clinical Trials Office
773-834-7424
Hedy Kindler, MD

**Michigan Cancer Research Consortium -- CCOP**

Ann Arbor, MI USA
734-434-4930
Phillip J. Stella, MD

**Kalamazoo - CCOP**

Kalamazoo, MI USA
269-373-7458
Raymond S. Lord, MD

**Metro Minnesota - CCOP**

St. Louis Park, MN USA
592-993-1517
Patrick J. Flynn, MD

**Ozarks Regional - CCOP**

Springfield, MO USA
417-269-4520
John W. Goodwin, MD

**University of Mississippi Cancer Clinic**

Jackson, MS USA
Robert D. Hamilton
601-984-5590

**Montana Cancer Consortium - CCOP**

Billings, MT USA
406-238-6290
Benjamin Marchello, MD

**Southeast Cancer Control Consortium - CCOP**

Winston-Salem, NC USA
910-777-3036
James M. Atkins, MD

**University of New Mexico Cancer Clinic**

Albuquerque, NM USA
Clinical Trials Office
505-272-6972

**Roswell Park Cancer Institute**

Buffalo, NY USA
Clinical Trials Office
877-275-7724

**Syracuse Hematology-Oncology Associate of Central New York - CCOP**

East Syracuse, NY USA
315-472-7504
Jeffrey J. Kirshner, MD
Masitinib, (AB1010)

Efficacy and Safety of Masitinib (AB1010) in Comparison to Imatinib in Patients With Gastro-Intestinal Stromal Tumour

**Phase:** 3  
**Stage:** First-line  
**Conditions:** Gastrointestinal Stromal Tumor  
**Drug Type:** KIT/PDGFRα inhibitor  
**Strategy:** Block KIT  
**NCT #:** [NCT00812240](#)

**Contact:** Centre Oscar Lambret  
Antoine Adenis, M.D.  
a-adenis@o-lambret.fr  
+33 (0)3 20 29 59 59  
**Hospital Jean Minjoz**  
Besancon, France

**Institut Bergonie**  
Bordeaux, France  
Binh Bui Nguyen, MD  
Centre Georges Francois Leclerc  
Dijon, France

**Centre Hospitalier Victor Jousselin**  
Dreux, France

**Centre Oscar Lambret - Lille**  
Lille, France  
Antoine Adenis, MD  
**Centre Leon Berard**  
Lyon, France  
Jean Yves-Blay, MD, PhD  
Centre Rene Gauducheau  
Nantes, France

**Hopital de la Source**  
Orleans, France

**Hopital Europen Georges Pompidou**  
Paris, France

**Hopital Robert Debre**  
Reims, France

**Hopital Charles Nicolle**  
Rouen, France

**Centre Rene Huguenin**  
Saint-Cloud, France

**Hopital Saint-Georges**  
Beirut, Lebanon

**American University Hospital**  
Beirut, Lebanon

**Middle East Institute of Health**  
Bsalim, Lebanon

**Hopital Saint-Joseph**  
Dora, Lebanon

**Hamoud Hospital**  
Saida, Lebanon

**MD Anderson - Orlando**  
Orlando, FL USA  
Centre Hospitalier Victor Jousselin  
Dreux, France

**Centre Rene Huguenin**  
Saint-Cloud, France

**Hopital Saint-Georges**  
Beirut, Lebanon

**American University Hospital**  
Beirut, Lebanon

**Middle East Institute of Health**  
Bsalim, Lebanon

**Hopital Saint-Joseph**  
Dora, Lebanon

**Hamoud Hospital**  
Saida, Lebanon
Nilotinib or Imatinib
Phase III, Open-Label Study of Nilotinib Versus Imatinib in GIST Patients

Phase: 3
Stage: First-line
Conditions: Gastrointestinal Stromal Tumor
Drug Type: KIT/PDGFRα inhibitor
Strategy: Block KIT
NCT #: NCT00785785
Contact: Novartis Pharmaceuticals

+1-800-340-6843

Universitätsklinik f. Innere Medizin Onkologische Ambulanz
Innsbruck, Austria
Annaliese Gachter
+43 512 504 23333
annaliese.gachter@uki.at
Eisterer Wolfgang, MD
Universitätsklinik f. Innere Medizin I
Vienna, Austria
Thomas Brodowicz, MD
+43-40400-4466
+43-40400-4685
Thomas Brodowicz, MD
Hotel Dieu du Quebec
Quebec, Canada
Ann Wright
1-418-691-2950
Felix Couture, MD
1-418-691-5225
Felix Couture, MD
Mount Sinai Hospital
Toronto, ON Canada
Martin Blackstein, MD
011-416-586-5371
Martin Blackstein, MD
Ottawa Regional Cancer Center University of Ottawa
Ottawa, Ontario Canada
Caroline Proulx, MD
613-737-7700 ext 70316
Tim Asmis, MD
Maisonneuve-Rosemont Hospital
Montreal, QC Canada
Jacinthe Lasalle, MD
514-252-3400 ext 4670
Lucas Sideris, MD
CHUM - Hospital Notre-Dame
Montreal, Quebec Canada
Chantal Gosselin
514-890-8000 ext. 24892
Denis Soulieres, MD
CHUS - Hospital Fleurimont
Sherbrooke, Quebec Canada
Brigitte Jean
1-819-346-1110 ext. 12872
Rami Kotb, MD
Centre Leon Berard
Lyon, France
+33-4-78-58-27-57
blay@lyon.fnclcc.fr
Jean Yves Cesne, MD
Institut Gustave-Roussy
Villejuif Cedex, France
+33-1-42-11-43-05
axel.lecsene@igr.fr
Axel Le Cesne, MD
Aichi Cancer Center Hospital
Aichi, Japan
Akira Sawaki, MD
+81-52-762-6111
jutaku.a@aichi-cc.jp
Akira Sawaki, MD
National Cancer Center Hospital East
Chiba, Japan
Toshihiko Doi, MD
+81-4-7133-1111
tdoi@east.ncc.go.jp
Toshihiko Doi, MD
Kyushu University Hospital
Fukuoka City, Japan
+81-92-641-1151
kakegi@surg2.med.kyushu.u.ac.jp
Yoshihiro Kakeji, MD
Hokkaido University Hospital
Hokkaido, Japan
Yoshito Komatsu
+81-11-706-5657
Yoshito Komatsu, MD
Kanagawa Cancer Center
Kanagawa, Japan
Haruhiko Cho, MD
+81-45-391-5791
Haruhiko Cho, MD
Kanagawa Cancer Center
Kanagawa, Japan
Haruhiko Cho, MD
+81-45-391-5791
Haruhiko Cho, MD
Kumamoto University Hospital
Kumamoto, Japan
Hideo Baba, MD
+81-96-344-2111
hdobaba@kumamoto-u.ac.jp
Hido Baba, MD
Niigata University Medical and Dental School
Niigata, Japan
Tatsuho Kanda, MD
+81-25-227-0372
kandat@med.niigata-u.ac.jp
Tatsuho Kanda, MD
National Hospital Organization - Osaka General Hospital
Osaka, Japan
Toshimasu Tsujinaka, MD
+81 6 6942 1331
toshi@onh.go.jp
Toshimasu Tsujinaka, MD
Osaka University Hospital
Osaka, Japan
Toshihiro Nishida, MD
+81-6-6879-5111
toshim@surg1.med.osaka-u.ac.jp
Toshihiro Nishida, MD
Shizuoka Cancer Center
Shizuoka, Japan
Yusuke Onozawa
+81-53-989-5222
yo.onozawa@scchr.jp
Yusuke Onozawa, MD
National Cancer Center Hospital
Tokyo, Japan
Yasuhide Yamada, MD
+81 33 542 5111
yamada@ncc.go.jp
Yasuhide Yamada, MD
Leiden University
Leiden, Netherlands
Jan Ouwerkerk
+31 71-5261965
j.ouwerkerk@lumc.nl
A. J. Gelderblom, MD
Consorti Hospitalari Parc Tauli
Barcelona, Spain
Jose G. Ruiz
+34-937-242-579
jgarciar@tauli.cat
Charles Pericay, MD
University Hospital La Paz
Madrid, Spain
Cristobal Belda-Iniesta, MD
+34-1-2071138
cbelda.hulp@salud.madrid.org
Cristobal Belda-Iniesta, MD
Dasatinib (BMS-354825)
Dasatinib as First-Line Therapy in Treating Patients With Gastrointestinal Stromal Tumors

Phase: 2
Stage: First-line
Conditions: Gastrointestinal Stromal Tumor
Drug Type: KIT/PDGFRα inhibitor + SRC inhibitor
Strategy: Block KIT + Block KIT Signal Path
NCT #: NCT00568750
Contact: See site contact info below

Centre Hospitalier Universitaire Vaudois
Lausanne, Switzerland
41-21-314-0150
Michael Montemurro, MD

Dasatinib as First-Line Therapy in Treating Patients With Gastrointestinal Stromal Tumors
Nilotinib

Treatment of Patients With Metastatic or Unresectable Gastrointestinal Stromal Tumors in First Line With Nilotinib. (OPEN)

- **Phase:** 2
- **Stage:** First-line
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** KIT/PDGFR inhibitor
- **Strategy:** Block KIT
- **NCT #:** NCT00756509
- **Contact:** Novartis Basel
  + 41 61 324 1111
  Site name unknown, Bad Saarow
  Bad Saarow, Germany
  Site name unknown, Milan
  Milan, Italy

Nilotinib or Imatinib

Nilotinib 800 Mg And Imatinib 800 Mg For The Treatment Of Patients With Gastrointestinal Stromal Tumors (Gist) Refractory To Gleevec-resistant

- **Phase:** 3
- **Stage:** Gleevec-resistant
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** KIT/PDGFR inhibitor
- **Strategy:** Block KIT
- **NCT #:** NCT00751036
- **Contact:** Novartis US: 1-800-340-6843
  Site name unknown Monteria
  Monteria, Colombia

Sunitinib

Safety And Efficacy Study Of Sunitinib Malate In Chinese Patients With Imatinib Resistant Or Intolerant Malignant

- **Phase:** 4
- **Stage:** Gleevec-resistant
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** KIT/PDGFR inhibitor
- **Strategy:** Block KIT
- **NCT #:** NCT00793871
- **Contact:** Pfizer Oncology Clinical Trial Information Service
  1-877-369-9753
  PfizerCancerTrials@emergin gmed.com
  Pfizer CT.gov Call Center
  1-800-718-1021
  Site name unknown Beijing 100035
  Beijing, China
  Site name unknown Beijing 100071
  Beijing, China
  Site name unknown, Beijing 100021
  Beijing, China
  Site name unknown, Nanjing 210002
  Nanjing, Jiangsu China

BIIB021 (CNF2024)

An Open-Label, 18FDG-PET Pharmacodynamic Assessment of the Effect of BIIB021 in Subjects With Gastrointestinal Stromal Tumors

- **Phase:** 2
- **Stage:** Gleevec-resistant
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** HSP90 inhibitor
- **Strategy:** Destroy KIT
- **NCT #:** NCT00618319
- **Contact:** Biogen Idec
  oncologyclinicaltrials@bioge nidec.com
  Site name unknown, Rochester
  Rochester, MN USA
  Memorial Sloan-Kettering Cancer Center
  New York, NY USA
  Robert Maki, MD
Nilotinib
Nilotinib in Advanced GIST

- Phase: 2
- Stage: Gleevec-resistant
- Conditions: Gastrointestinal Stromal Tumor
- Drug Type: KIT/PDGFRA inhibitor
- Strategy: Block KIT
- NCT #: NCT00782834
- Contact: See site contact info below

Nilotinib
Phase II Study Aiming to Evaluate the Efficacy and Safety of Nilotinib Patients With Gastrointestinal Stromal Tumors (GIST) Resistant or Phase: 2
Stage: Gleevec-resistant
Conditions: Gastrointestinal Stromal Tumor
Drug Type: KIT/PDGFRA inhibitor
Strategy: Block KIT
NCT #: NCT00633295
Contact: Novartis Basel
41 61 324 1111
Site name unknown, Tel Aviv
Tel Aviv, Israel
Site name unknown, Tel Hashomer
Tel Hashomer, Israel

Sorafenib (Nexavar, BAY 43-9006)
Sorafenib in Treating Patients With Malignant Gastrointestinal Stromal Tumor That Progressed During or After Previous Treatment With

- Phase: 2
- Stage: Gleevec-resistant
- Conditions: Gastrointestinal Stromal Tumor
- Drug Type: KIT/PDGFRA inhibitor+
  VEGF inhibitor (TKI) + RAF inhibitor
- Strategy: Block KIT + Block KIT Signal Path
- NCT #: NCT00265798
- Contact: Clinical Trials Office - University of Chicago Cancer Research
  773-834-7424
University of Chicago
Chicago, IL USA
Clinical Trials Office, 773-834-7424
Hedy Kindler, MD

Imatinib + Sunitinib
Imatinib Mesylate and Sunitinib in Treating Patients With Gastrointestinal Stromal Tumors

- Phase: 1
- Stage: Gleevec-resistant
- Conditions: Gastrointestinal Stromal Tumor
- Drug Type: KIT/PDGFRA inhibitor
- Strategy: Block KIT
- NCT #: NCT00573404
- Contact: Vanderbilt-Ingram Cancer Center-Cool Springs
  Franklin, TN USA
  615 343-4128
Jordan Berlin
Vanderbilt-Ingram Cancer Center at Franklin
Franklin, TN USA
615 343-4128
Jordan Berlin

Dasatinib (BMS-354825)
Trial of Dasatinib in Advanced Sarcomas

- Phase: 2
- Stage: Gleevec-resistant
- Conditions: Gastrointestinal Stromal Tumor
- Drug Type: KIT/PDGFRA inhibitor + SRC inhibitor
- Strategy: Block KIT + Block KIT Signal Path
- NCT #: NCT00464620
- Contact: Kathleen Granlund
ekgranlund@sarctrials.org
734-930-7607

Arkansas Children's Hospital
Little Rock, AR USA
Bryce Warren
WarrenBryceA@uams.edu
Kimo Stine
City of Hope
Duarte, CA USA
Neeti Arora
626-256-4673 ext. 63019
NArora@coh.org
Warren Chow, MD
Everolimus

Treatment of Patients With RAD001 Who Have Progressive Sarcoma

- **Phase:** 2
- **Stage:** Gleevec-resistant
- **Conditions:** Sarcoma
- **Drug Type:** mTOR inhibitor
- **Strategy:** Block KIT Signal Path
- **NCT #:** NCT00767819
- **Contact:** Novartis Pharmaceuticals
  +1 800-340-6843

**Site name unknown, Berlin**
- Berlin, Germany

**Site name unknown, Dusseldorf**
- Dusseldorf, Germany

**Site name unknown, Mannheim 68135**
- Mannheim, Germany

**Site name unknown, Munchen**
- Munchen, Germany

**Site name unknown, Milan**
- Milan, Italy

---

**Cedars-Sinai Outpatient Cancer Center**
Los Angeles, CA USA
Chi Vu
310-423-2133
CVu@csocc.com
Charles Forscher, MD

**Stanford Cancer Center**
Palo Alto, CA USA
Maria Ahem
650-725-6413
mahem@stanford.edu

**Charles Forscher, MD**
Stanford Cancer Center
Palo Alto, CA USA
Maria Ahem
650-725-6413
mahem@stanford.edu

**Kristen Ganjoo, MD**
Sarcoma Oncology Center
Santa Monica, CA USA
Vicky Chua
(310) 552-9999
vikychua@aol.com
Sant Chawla, MD

**Washington Cancer Institute**
Washington, DC USA
Christina Sheeran,
202 877-5371
christina.m.
sheeran@medstar.net
Dennis A. Priebat, MD

**University of Iowa Hospitals and Clinics**
Iowa City, IA USA
Melanie Frees, RN
319-356-1228
melanie-frees@uiowa.edu
Mohammed Milhem, MD

**Kootenai Cancer Center**
Coeur d’Alene, ID USA
Sheryl Goldon
208-666-2093
golden@kmc.org
Brian Samuels, MD

**Periitana Oncology Hematology Associates**
Philadelphia, PA USA
Deb Riordan, RN, BS
215-829-6712
debriordan@pennoncology.com
Kirsten Leu, MD

**Maryland Oncology Hematology**
College Park, MD USA
Dennis Dorn, MD
301-739-6117
dennis.dorn@uhsp.edu
Stuart Schiffer, MD, PhD

**Indiana University Simon Cancer Center**
Indianapolis, IN USA
Kristen Potter, MS
317-278-6616
kpotter@iuui.edu
Daniel Rushing, MD

**Massachusetts General Hospital**
Boston, MA USA
Anthony Thomas
617-643-5411
athomas2@partners.org
Edwin Choy, MD

**Dana Farber Cancer Institute**
Boston, MA USA
Sarah Solomon
617-582-7503
ssolomon1@partners.org
James Butynski, MD

**Johns Hopkins Sidney Kimmel Comp Cancer Center**
Baltimore, MD USA
Adult Oncology, 410-955-8804
Pediatric Oncology, 410-955-8751
David Loeb, MD, PhD

**University of Michigan**
Ann Arbor, MI USA
Gino Metko
734-647-2095
ginom@med.umich.edu
Scott Schuetze, MD, PhD

**Pennsylvania Oncology Hematology**
Philadelphia, PA USA
Lynne Frydrych
412-623-4036
frydrychlm2@upmc.edu
Hussein Tawbi, MD, MSc

**MD Anderson Cancer Center**
Houston, TX USA
Joanne Gigstad
713-563-0510
jgigstad@mdanderson.org
Shreyas Patel, MD
**Doxorubicin + Flavopiridol**
*Doxorubicin and Flavopiridol in Treating Patients With Metastatic or Recurrent Sarcoma That Cannot Be Removed By Surgery*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Gastrointestinal Stromal Sarcoma
- **Drug Type:** Transcription inhibitor + Chemotherapy
- **Strategy:** Freeze the cell division cycle
- **NCT #:** NCT00098579
- **Contact:** See site contact info below

**Multi-bacteria vaccine (MBV)**
*A Phase 1 Study of Mixed Bacteria Vaccine (MBV) in Patients With Tumors Expressing NY-ESO-1 Antigen.*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** Immune stimulate
- **Strategy:** Stimulate the immune system
- **NCT #:** NCT00623831
- **Contact:** See site contact info below

**Imatinib + IL-2**
*Imatinib + IL-2*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** KIT inhibitor + Immune stimulate
- **Strategy:** Block KIT + Stimulate the immune system
- **NCT #:** NCT00098579
- **Contact:** See site contact info below

**SF1126**
*A Phase I Open Label, Safety, Pharmacokinetic and Pharmacodynamic Dose Escalation Study in SF1126, a PI Kinase (PI3K)*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** PI3K inhibitor
- **Strategy:** Block KIT Signal Path
- **NCT #:** NCT00907205
- **Contact:** See site contact info below

**AUY922**
*Phase I-II Study to Determine the Maximum Tolerated Dose (MTD) of AUY922 in Advanced Solid Malignancies, and Efficacy in HER2*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** HSP90 inhibitor
- **Strategy:** Destroy KIT
- **NCT #:** NCT00526045
- **Contact:** Novartis Pharmaceuticals

Additional contact information for various institutions and researchers is included throughout the document.
**BGT226**

*A Phase I/II Study of BGT226 in Adult Patients With Advanced Solid Malignancies Including Patients With Advanced Breast Cancer*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** mTOR inhibitor, PI3K inhibitor
- **Strategy:** Block KIT Signal Path
- **NCT #:** [NCT00600275](#)
- **Contact:** Novartis
  800 340-6843

**Dana Farber Cancer Institute**

Boston, MA USA
706-721-2505
tsamuel@mcg.edu
Thomas Samuel, M.D.

**Dana Farber Cancer Institute**

Boston, MA USA
617 632-5053
stephen_hodi@dfci.harvard.edu
Stephen Hodi, MD, PhD

**Massachusetts General Hospital**

Boston, MA USA
617-726-6225
nisaac1@partners.org
Stephen Isakoff, MD

**Nevada Cancer Institute**

Las Vegas, NV USA
Dianna Tercan
(702) 822-5483
Lin-Chi Chen, M.D., Ph.D.

**Cancer Therapy and Research Center**

San Antonio, TX USA
Epp Goodwin
210-450-5798
Francis Giles, MD

---

**MP470**

*Safety Study to Determine the Maximum Tolerated Dose, Pharmacokinetics and Pharmacodynamics of Oral MP470, in Treating Patients With Unresectable or Metastatic Solid Tumor or Lymphoma*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Advanced Stage Solid Tumors
- **Drug Type:** KIT/PDGFRA inhibitor
- **Strategy:** Block KIT
- **NCT #:** [NCT00504205](#)
- **Contact:** TGen Clinical Research Services Cancer Care Coordinator
  480-323-1255

---

**Virginia Piper Cancer Center**

Scottsdale, AZ USA
Raoul Tibes, MD, 480-323-1350

---

**South Texas Accelerated Research Therapeutics (START)**

San Antonio, TX USA
Anthony Tolcher, MD, (210) 593-5255
Note: Contact number is not verified.

Anthony Tolcher, MD
**SNX-5422**

*SNX-5422 in Treating Patients With Solid Tumor or Lymphoma That Has Not Responded to Treatment*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** HSP90 inhibitor
- **Strategy:** Destroy KIT
- **NCT #:** [NCT00644072](https://www.clinicaltrials.gov/ct2/show/NCT00644072)
- **Contact:** Warren Grant Magnuson Clinical Center, Bethesda, MD USA

**Vorinostat + Bortezomib**

*Vorinostat and Bortezomib in Treating Patients With Metastatic or Unresectable Solid Tumors*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** HDAC inhibitor + Proteasome inhibitor
- **Strategy:** Inhibit protein translation + Unblock cell death genes
- **NCT #:** [NCT00227513](https://www.clinicaltrials.gov/ct2/show/NCT00227513)
- **Contact:** Carbone Cancer Center, University of Wisconsin, Madison, WI USA

**AMG 479 + AMG 655**

*AMG 655 in Combination With AMG 479 in Advanced, Refractory Solid Tumors*

- **Phase:** 2
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** IGF1R inhibitor + DR5 Inhibitor
- **Strategy:** Block related tumor signal paths
- **NCT #:** [NCT00819169](https://www.clinicaltrials.gov/ct2/show/NCT00819169)
- **Contact:** Amgen Call Center, 866-572-6436

**Vorinostat + Bortezomib**

*Vorinostat and Bortezomib in Treating Patients With Metastatic or Unresectable Solid Tumors*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** HDAC inhibitor + Proteasome inhibitor
- **Strategy:** Inhibit protein translation + Unblock cell death genes
- **NCT #:** [NCT00227513](https://www.clinicaltrials.gov/ct2/show/NCT00227513)
- **Contact:** Carbone Cancer Center, University of Wisconsin, Madison, WI USA

**AT13387**

*Phase 1 Study of HSP90 inhibitor AT13387 in solid tumors*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** HSP90 inhibitor
- **Strategy:** Destroy KIT
- **NCT #:** [NCT00878423](https://www.clinicaltrials.gov/ct2/show/NCT00878423)
- **Contact:** Andrew Wolanski, 617-632-6623, Andrew_Wolanski@dfci.harvard.edu

**BAY 73-4506**

*Phase I study of BAY 73-4506*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** KIT/PDGFRA inhibitor VEGFR inhibitor (TKI)
- **Strategy:** Block KIT
- **NCT #:** [See site contact info below](https://www.mdanderson.org/research/trials/73-4506)
- **Contact:** See site contact info below

**Site names unknown, Barcelona 08036 Barcelona, Spain**

**Site name unknown, Indianapolis**

**Site name unknown, Detroit**

**Site name unknown, Santa Monica 90403 Santa Monica, CA USA**

**University of Chicago**

Chicago, IL USA

Clinical Trials Office, 773-834-7424

Hedy Kindler, MD

**Site name unknown, Indianapolis**

**Site name unknown, Detroit**

**Site name unknown, Indianapolis, IN USA**

**Site name unknown, Santa Monica**

**Site name unknown, Detroit**

**Site name unknown, MD Anderson Cancer Center**

Houston, TX USA

Clinical Trials Office, 713-792-3245

Jon Trent, MD, PhD

**South Texas Accelerated Research Therapeutics (START)**

San Antonio, TX USA

Tracy Dufresne, RN

210-593-5265

tracy.dufresne@start.stoh.com
BEZ235
A Phase I/II Study of BEZ235 in Patients With Advanced Solid Malignancies Enriched by Patients With Advanced Breast Cancer

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: mTOR inhibitor, PI3K inhibitor
Strategy: Block KIT Signal Path
NCT #: NCT00620594
Contact: Novartis
862-778-8300

Nevada Cancer Institute
Las Vegas, NV USA
Dianna Tercan
(702) 822-5483
Wolfram Samlowski, M.D.

Sarah Cannon Research Institute
Nashville, TN USA
615-329-7274
hburriss@tnonc.com
Howard A. Burris, III MD

BIIB022
Phase I Study of BIIB022 (Anti-IGF-1R Monoclonal Antibody) in Relapsed/Refractory Solid Tumors

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: IGF1R inhibitor
Strategy: Block related tumor signal paths
NCT #: NCT00555724
Contact: Biogen Idec
oncologyclinicaltrials@biogenidec.com
Site name unknown, Los Angeles, CA
Los Angeles, CA USA

University of Colorado
Aurora, CO USA
Sarah Eppers
720-848-0052
SARAH.EPPERS@ucdenver.edu
Stephen Leong

Fox Chase Cancer Center
Philadelphia, PA USA
Kathleen Lear, RN, OCN, CCRP
Phone: 215-214-1511
Email: kathleen.lear@fccc.edu
Roger Cohen, MD

BKM120
A Phase IA, Multi-Center, Open-Label, Dose-Escalation Study of BKM120, Administered Orally on a Continuous Daily Dosing Schedule

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: HSP90 inhibitor
Strategy: Block KIT Signal Path
NCT #: NCT00725933
Contact: See site contact info below

Sarah Cannon Research Institute
Nashville, TN USA
615-329-SCRI (7274)

BIIB028

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: HSP90 inhibitor
Strategy: Destroy KIT
NCT #: NCT00725933
Contact: Biogen Idec
oncologyclinicaltrials@biogenidec.com

Site name unknown, Los Angeles, CA
Los Angeles, CA USA

MD Anderson Cancer Center
Houston, TX USA
Clinical Trials Office - M.D. Anderson Cancer Center,
713-792-3245
Jon Trent, MD, PhD

BIIB021 (CNF2024)
Once or Twice Daily Administration of BIIB021 to Subjects With Advanced Solid Tumors

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: HSP90 inhibitor
Strategy: Destroy KIT
NCT #: NCT00618735
Contact: Biogen Idec
oncologyclinicaltrials@biogenidec.com

Premier Oncology, Santa Monica
Santa Monica, CA USA

South Texas Accelerated Research Therapeutics (START)
San Antonio, TX USA

San Deigo Pacific Oncology and Hematology Associates
Encinitas, CA USA
Karen Brady, RN MSN
760-752-3340
kbrady@premiereoncology.com
Richard Just, M.D.
**BMS-754807**

*Multiple Dose Study In Cancer Patients: Safety and Tolerability of BMS-754807 in Advanced or Metastatic Solid Tumors*

| Phase: 1 |
| Stage: Gleevec-resistant |
| Conditions: Solid Tumors |
| Drug Type: IGF1R inhibitor |
| Strategy: Block related tumor signal paths |
| NCT #: NCT00569036 |
| Contact: For site information outside the USA please email: Clinical.Trials@bms.com First line of email MUST contain NCT# & Site#. |

**Site name unknown, East Melbourne**
East Melbourne, Australia
Site # 003

**Site name unknown, Footscray, Australia**
Footscray, Victoria Australia
Site # 004

**Site name unknown, Heidelberg Australia**
Heidelberg, Victoria Australia
Site # 002

**Site name unknown, Parkville, Australia**
Parkville, Victoria Australia
Site #001

---

**GDC-0941**

*A Study of GDC-0941 in Patients With Locally Advanced or Metastatic Solid Tumors for Which Standard Therapy Either Does Not Exist or*...

| Phase: 1 |
| Stage: Gleevec-resistant |
| Conditions: Solid Tumors |
| Drug Type: PI3K inhibitor |
| Strategy: Block KIT Signal Path |
| NCT #: NCT00876109 |
| Contact: See site contact info below |

**TGen Clinical Research Services**
Scottsdale, AZ USA
Lynne Hull
480-323-1071
LHull@SHC.org
Daniel D. Hoff, MD

**Dana Farber Cancer Institute**
Boston, MA USA
Melissa Hohos
617 632-2201
mehohos@partners.org
George Demetri, MD, PhD

**Karmanos Cancer Institute**
Detroit, MI USA
Jie Zhang
313-576-9365
zhangj@karmanos.org

---

**IMC-A12 + CCI-779**

*Cixutumumab and Temsirolimus in Treating Young Patients With Solid Tumors That Have Recurred or Not Responded to Treatment*

| Phase: 1 |
| Stage: Gleevec-resistant |
| Conditions: Solid Tumors |
| Drug Type: IGF1R inhibitor + mTOR Inhibitor |
| Strategy: Block related tumor signal paths |
| NCT #: NCT00880282 |
| Contact: |

**Children's Hospital of Orange County**
Orange, CA USA
Violet Shen
714-532-8636

**Children's National Medical Center**
Washington, DC USA
Clinical Trials Office
202-884-2549

**Masonic Cancer Center at University of Minnesota**
Minneapolis, MN USA
Clinical Trials Office
612-624-2620

**Cincinnati Children's Hospital Medical Center**
Cincinnati, OH USA
Clinical Trials Office
513-636-2799

---

**GDC-0941**

*A Study of GDC-0941 in Patients With Locally Advanced or Metastatic Solid Tumors or Non-Hodgkin's Lymphoma for Which Standard Therapy Does Not Exist or*...

| Phase: 1 |
| Stage: Gleevec-resistant |
| Conditions: Solid Tumors |
| Drug Type: PI3K inhibitor |
| Strategy: Block KIT Signal Path |
| NCT #: NCT00876122 |
| Contact: See site contact info below |

**Royal Marsden Hospital**
London, UK
Krunal Shah
0208 722 4005
Krunal.Shah@icr.ac.uk
IMC-A12 + CCI-779
Monoclonal Antibody IMC-A12 and Temsirolimus in Treating Patients With Locally Advanced or Metastatic Cancer

**Phase:** 1  
**Stage:** Gleevec-resistant  
**Conditions:** Solid Tumors  
**Drug Type:** IGF1R inhibitor + mTOR Inhibitor  
**Strategy:** Block related tumor signal paths  
**NCT #:** NCT00678223  
**Contact:** 
Aung Naing, MD  
713-792-3245  
Aung Naing, MD  
MD Anderson Cancer Center  
Houston, TX USA  
Clinical Trials Office - M.D. Anderson Cancer Center,  
713-792-3245  
Aung Naing, MD

IPI-493
A Phase I Dose Escalation Study of IPI-493

**Phase:** 1  
**Stage:** Gleevec-resistant  
**Conditions:** Solid Tumors  
**Drug Type:** HSP90 inhibitor  
**Strategy:** Destroy KIT  
**NCT #:** NCT00724425  
**Contact:** See site contact info below  
Premier Oncology, Sacramento, CA  
Patrick Shannon, RN  
707-546-1595  
pshannon@premiereoncology.com  
Jill Schmidt  
301-398-0000  
schmidtj@medimmune.com  
Lorena DeRienzo  
301-398-0000  
de-rienzol@medimmune.com  
MD Anderson Cancer Center  
Houston, TX USA  
Clinical Trials Office - M.D. Anderson Cancer Center,  
713-792-3245  
Aung Naing, MD

KW2450
Safety Study to Evaluate KW-2450 in Subjects With Advanced Solid Tumor

**Phase:** 1  
**Stage:** Gleevec-resistant  
**Conditions:** Solid Tumors  
**Drug Type:** IGF1R inhibitor  
**Strategy:** Block related tumor signal paths  
**NCT #:** NCT00921336  
**Contact:** Danyel Davis  
(609) 919-1100  
ddavis@kyowa-kirin-pharma.com  
Neil Senzer  
(609) 919-1100  
nrao@kyowa-kirin-pharma.com  
Memorial Sloan-Kettering Cancer Center  
New York, NY USA

MEDI-573
A Dose-Escalation Study to Evaluate the Safety, Tolerability, and Antitumor Activity of MEDI-573 in Subjects With Advanced Solid

**Phase:** 1  
**Stage:** Gleevec-resistant  
**Conditions:** Solid Tumors  
**Drug Type:** IGF1R inhibitor  
**Strategy:** Block related tumor signal pathways  
**NCT #:** NCT00816361  
**Contact:** 
Jill Schmidt  
301-398-0000  
schmidtj@medimmune.com  
Lorena DeRienzo  
301-398-0000  
de-rienzol@medimmune.com  
Mayo Clinic, Jacksonville, FL USA  
Michele Maharaj  
904-953-6136  
maharaj.michele@mayo.edu  
Michael E. Menefee, MD
## OSI-906

**Phase 1 Study of Continuous OSI -906 Dosing**

<table>
<thead>
<tr>
<th>Phase: 1</th>
<th>Stage: Gleevec-resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions: Solid Tumors</td>
<td></td>
</tr>
<tr>
<td>Drug Type: IGF1R inhibitor</td>
<td></td>
</tr>
<tr>
<td>Strategy: Block related tumor signal paths</td>
<td></td>
</tr>
<tr>
<td>NCT #: NCT00514007</td>
<td></td>
</tr>
<tr>
<td>Contact: OSIP Medical Information 800.572.1932 ext 7821 <a href="mailto:medical-information@osip.com">medical-information@osip.com</a></td>
<td></td>
</tr>
</tbody>
</table>

**Department of Cancer Therapeutics, Institute of Cancer Research**
Sutton, Surrey UK

**MD Anderson Cancer Center**
Houston, TX USA
Edward Kim, MD

## PX-866

**Phase 1 Trial of Oral PX-866**

<table>
<thead>
<tr>
<th>Phase: 1</th>
<th>Stage: Gleevec-resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions: Solid Tumors</td>
<td></td>
</tr>
<tr>
<td>Drug Type: PI3K inhibitor</td>
<td></td>
</tr>
<tr>
<td>Strategy: Block KIT Signal Path</td>
<td></td>
</tr>
<tr>
<td>NCT #: NCT00726583</td>
<td></td>
</tr>
<tr>
<td>Contact: See site contact info below</td>
<td></td>
</tr>
</tbody>
</table>

**University of Colorado**
Aurora, CO USA
Sharon hecker 720-848-0667 sharon.hecker@ucdenver.edu
Antonio Jimeno, MD

**MD Anderson Cancer Center**
Houston, TX USA
Rhonda Clement 713-563-3559 rclement@mdanderson.org
Roy Herbst, MD

## PX-478

**Phase 1 Trial of PX-478**

<table>
<thead>
<tr>
<th>Phase: 1</th>
<th>Stage: Gleevec-resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions: Solid Tumors</td>
<td></td>
</tr>
<tr>
<td>Drug Type: HIF-1α inhibitor</td>
<td></td>
</tr>
<tr>
<td>Strategy: Block related tumor signal paths Block tumor blood vessel</td>
<td></td>
</tr>
<tr>
<td>NCT #: NCT00522652</td>
<td></td>
</tr>
<tr>
<td>Contact: See site contact info below</td>
<td></td>
</tr>
</tbody>
</table>

**TGen Clinical Research Services**
Scottsdale, AZ USA
Lynne Hull 480-323-1071 lhull@shc.org
Daniel D. VonHoff, MD

**MD Anderson Cancer Center**
Houston, TX USA
Hala Abdulkadir 713-792-9944 habdulka@mdanderson.org
Roy S. Herbst, PhD

## R1507

**A Multiple Ascending Dose Study of R1507 in Children and Adolescents With Advanced Solid Tumors**

<table>
<thead>
<tr>
<th>Phase: 1</th>
<th>Stage: Gleevec-resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions: Solid Tumors</td>
<td></td>
</tr>
<tr>
<td>Drug Type: IGF1R inhibitor</td>
<td></td>
</tr>
<tr>
<td>Strategy: Block related tumor signal paths</td>
<td></td>
</tr>
<tr>
<td>NCT #: NCT00560144</td>
<td></td>
</tr>
<tr>
<td>Contact: Hoffmann-La Roche Please reference Study ID Number: NO21200 973-235-5000 800-526-6367 (US only)</td>
<td></td>
</tr>
</tbody>
</table>

**Site name unknown, Denver 80218**
Denver, CO USA

**Site name unknown, Bethesda 20982**
Bethesda, MD USA

**Memorial Sloan-Kettering Cancer Center**
New York, NY USA
212-639-8267 Dr. Tanya Trippett
SNX-5422
Safety and Pharmacology of SNX-5422 Mesylate in Subjects With Refractory Solid Tumor Malignancies

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: HSP90 inhibitor
Strategy: Destroy KIT
NCT #: NCT00647764
Contact: Pfizer Oncology Clinical Trial Information Service
1-877-369-9753
PfizerCancerTrials@emergin gmed.com
Pfizer CT.gov Call Center
1-800-718-1021
Site name unknown, Bethesda 20982
Bethesda, MD USA

Sorafenib + Vorinostat
Phase I Vorinostat + Sorafenib in Patients With Advanced Solid Tumors

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: HDAC inhibitor + KIT/PDGFRA inhibitor
Strategy: Block KIT + Unblock cell death genes + Destroy KIT
NCT #: NCT00635791
Contact: See site contact info below
University of Colorado
Aurora, CO USA
Stacy Grolnic
720-848-0655
stacy.grolnic@uchsc.edu
David Ross Camidge MD

STA-9090
Study of STA-9090, Administered Once-Weekly in Patients With Solid Tumors

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: HSP90 inhibitor
Strategy: Destroy KIT
NCT #: NCT00687934
Contact: See site contact info below
Premier Oncology, Santa Monica
Santa Monica, CA USA
310-633-8400
Lee Rosen, MD
US Oncology - Dayton Oncology & Hematology
Kettering, OH USA
robert.raju@usoncology.com
(937)293-1622
Robert Raju, MD

STA-9090
Study of STA-9090, Administered Twice-Weekly in Patients With Solid Tumors

Phase: 1
Stage: Gleevec-resistant
Conditions: Solid Tumors
Drug Type: HSP90 inhibitor
Strategy: Destroy KIT
NCT #: NCT00688116
Contact: See site contact info below
Dana Farber Cancer Institute
Boston, MA USA
Melissa Hohos, RN, 617-632-2201
Geoffrey Shapiro, MD, PhD
Massachusetts General Hospital
Boston, MA USA
Pilar De La Roche Mur 617-632-5841

Beth Israel Deaconess Medical Center
Boston, MA USA
Pilar De La Roche Mur 617-632-5841
**Sunitinib + CP-751,871**

*Phase 1 Study of CP-751,871 in Combination With Sunitinib in Patients With Advanced Solid Tumors*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** KIT/PDGFRA inhibitor + IGFIR inhibitor
- **Strategy:** Block KIT + Block related tumor signal paths
- **NCT #:** NCT00729833
- **Contact:** EmergingMed
  - (877) 369-9753
  - PfizerCancerTrials@emerginmed.com
  - Pfizer CT.gov Call Center
  - 1-800-718-1021

**Premier Oncology, Santa Monica**

Santa Monica, CA USA
310 633-8400
Lee Rosen

**South Texas Accelerated Research Therapeutics (START)**
San Antonio, TX USA

---

**XL147**

*Study of the Safety and Pharmacokinetics of XL147 in Adults With Solid Tumors*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** PI3K inhibitor
- **Strategy:** Block KIT Signal Path
- **NCT #:** NCT00486135
- **Contact:** Exelixis Contact Line
  - 866-939-4041

**Hospital Vall d'Hebron**
Barcelona, Spain
Gemma Sala
+34 93 489 4158
gsala@vhebron.net
Jose Baselga, MD, PhD

**Dana Farber Cancer Institute**
Boston, MA USA
Pilar de la Rocha Mur
617-632-5841
pilar_DelRochaMur@dfci.harvard.edu
Geoffrey Shapiro, MD

**Mary Crowley Medical Research Center (Baylor)**
Dallas, TX USA
J.R. Dolan
214-658-1943
Gerald Edelman MD, PhD

---

**XL765**

*Study of the Safety and Pharmacokinetics of XL765 in Adults With Solid Tumors*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** PI3K inhibitor
- **Strategy:** Block related tumor signal paths
- **NCT #:** NCT00485719
- **Contact:** Exelixis Contact Line
  - 866-939-4041

**Hospital Vall d'Hebron**
Barcelona, Spain
Gemma Sala
+34 93 489 4158
gsala@vhebron.net
Jose Baselga, MD, PhD

**Karmanos Cancer Institute**
Detroit, MI USA
Theresa Laeder
313-576-9386
Patricia LoRusso, DO

**South Texas Accelerated Research Therapeutics (START)**
San Antonio, TX USA
Gina Mangold, MBA
210-413-3594
gmangold@start.stoh.com
Kyriakos Papadopoulos, MD

---

**XL228**

*Study of XL228 Administered Intravenously to Subjects With Advanced Malignancies*

- **Phase:** 1
- **Stage:** Gleevec-resistant
- **Conditions:** Solid Tumors
- **Drug Type:** IGFIR inhibitor
- **Strategy:** Block related tumor signal paths
- **NCT #:** NCT00526838
- **Contact:** Exelixis Contact Line
  - 1-866-939-4041

**University of Michigan**
Ann Arbor, MI USA
Nabeela Iqbal
734-232-0759
David Smith, MD

---

**Duke University**
Durham, NC USA
Sharon Norman
919-681-5257
Herb Horowitz, MD

---

**Hospital Vall d'Hebron**
Barcelona, Spain
Gemma Sala
+34 93 489 4158
gsala@vhebron.net
Jose Baselga, MD, PhD

**Karmanos Cancer Institute**
Detroit, MI USA
Theresa Laeder
313-576-9386
Patricia LoRusso, DO

**South Texas Accelerated Research Therapeutics (START)**
San Antonio, TX USA
Gina Mangold, MBA
210-413-3594
gmangold@start.stoh.com
Kyriakos Papadopoulos, MD

---

22
<table>
<thead>
<tr>
<th>Treatment Stage:</th>
<th>Palliative</th>
<th>Stable Disease</th>
</tr>
</thead>
</table>

### Radiation

*Radiation Therapy as Palliative Treatment of GIST (GIST-RT)*

- **Phase:** 1
- **Stage:** Palliative
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** None
- **Strategy:** Radiation
- **NCT #:** NCT00515931
- **Contact:** See site contact info below

**Helsinki University Central Hospital**
Helsinki, Finland
947173208 Ext. 358
heikki.joensuu@hus.fi
Heikki Joensuu, MD

---

### Sunitinib + Radiation

*Sutent and Radiation as Treatment for Limited Extent Metastatic Cancer*

- **Phase:** 2
- **Stage:** Palliative
- **Conditions:** Any type of Cancer
- **Drug Type:** KIT/PDGFRA inhibitor
- **Strategy:** Block KIT
- **NCT #:** NCT00463060
- **Contact:** See site contact info below

**Mount Sinai School of Medicine**
New York, NY USA
212-241-7503
johnny.kao@mountsinai.org
Johnny Kao, MD

---

### Imatinib

*A phase III randomized study evaluating surgery of residual disease in patients with metastatic gastro-intestinal stromal tumor*

- **Phase:** 3
- **Stage:** Stable Disease
- **Conditions:** Gastrointestinal Stromal Tumor
- **Drug Type:** KIT/PDGFRA inhibitor
- **Strategy:** Block KIT
- **NCT #:**
- **Contact:** Anne Kirkpatrick
  Project Manager - EORTC, Brussels, Belgium
  anne.kirkpatrick@eortc.be
  +32 2 7741691

**Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital**
Amsterdam, Netherlands