



AMERICAN COLLEGE OF SURGEONS ONCOLOGY GROUP

ACOSOG Z9001

A Phase III Randomized Double-blind Study of Adjuvant STI571 (Imatinib, Gleevec™) Versus Placebo in Patients Following the Resection of Primary Gastrointestinal Stromal Tumor (GIST)

Frequently Asked Questions and Contact List*

*(see final page)

Section I: Basic Information

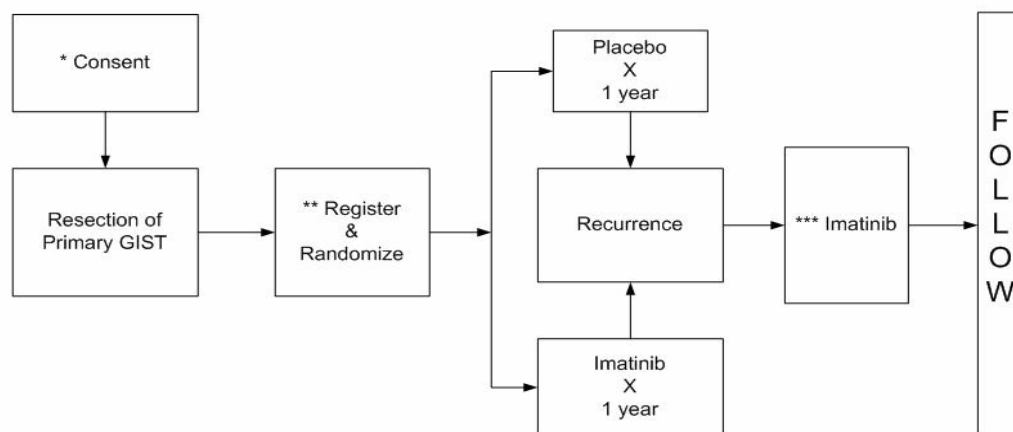
What is the Z9001 study and what are its goals?

Z9001 is a large North American-based Cooperative Inter-Group trial sponsored by the American College of Surgeons Group (ACOSOG). It is open to members of the Southwest Oncology Group (SWOG), Eastern Cooperative Oncology Group (ECOG), Cancer and Leukemia Group B (CALGB), the National Cancer Institute of Canada (NCIC) Clinical Trials Program, and others.

The trial is evaluating the activity and safety of imatinib as postoperative adjuvant therapy for resected gastrointestinal stromal tumors (GISTs). The trial is a phase III double-blind randomized trial comparing Imatinib vs. Placebo. The primary endpoint is recurrence free survival.

The schema of the protocol is as follows:

Z9001



* Patients can be consented (including HIPPA authorization) either before or after complete resection of GIST.

** Patients must be registered from a minimum of 14 days following surgery to a maximum of 70 days following surgery. Therapy must be initiated prior to 84 days from surgery.

*** At the discretion of the treating investigator.

Why did ACOSOG halt this study?

The decision to suspend enrollment was made by the study leadership and the ACOSOG's Data Monitoring Committee (DMC) based on the observation that the outcomes on the Imatinib (STI571) arm are significantly better than on the control Placebo arm. The decision was based on follow-up information on over 600 patients that was provided to the DMC. Based on these findings, the ACOSOG DMC recommended that the results of the Z9001 trial be made public.

What is the extent of the benefit?

Approximately 97% of patients in the study who received one year of imatinib (STI571 or Imatinib, Gleevec™) after surgery did not have a recurrence of their cancer as compared to 83% of patients who received one year of placebo. These results were highly statistically significant. In addition, imatinib therapy was well tolerated by most patients enrolled in the study and the types of side effects observed in this trial were similar to those observed in other clinical trials with imatinib.

Section II: What Happens Now?

A. Summary

- **All patients will be unblinded.**
- **All patients will continue with follow-up as required by protocol.**
- **It is the responsibility of the physician to discuss these results with the patient and to determine the appropriate course of action for the patient.**
- **A “Crossover and Notification Form” must be completed for each patient and faxed directly to ACOSOG at (919) 668-7156.**
- **Patients who have signed the informed consent document as of April 12, 2007 will be permitted to enter the trial until 5:00 PM EDT on April 18, 2007. All newly enrolled patients will be assigned to one year of imatinib.**

B. IRB Notification

You will need to notify your IRB of this information. Please follow all applicable procedures regarding IRB submission of the patient letter at your site; however, communication of this information to patients as soon as possible with subsequent unblinding and cross-over from placebo to imatinib therapy for patients does not require prior IRB approval. A future amendment to update the protocol with these changes also will be provided.

C. Patient Notification

1. All investigators who participated in the trial will receive notification of whether their patients were/are taking imatinib or placebo. Investigators will be contacted separately by the ACOSOG Coordinating Center (for ACOSOG investigators) or by the Cancer Trials Support Unit (for investigators participating via the CTSU) with information regarding patient treatment assignments. The treatment assignments will be sent via Federal Express on Friday, April 13th, 2007 and should be expected to arrive on Monday, April 16th, 2007. It is the responsibility of each investigator to notify each of their patients of their treatment assignment. Physician and patient contact letter templates are available on the ACOSOG website at www.acosog.org.
2. Patients currently being treated with imatinib should continue to receive the full one-year duration of therapy following the current protocol guidelines and procedures.
3. Patients who were receiving treatment with Placebo as of April 1st, 2007 may elect to receive one full year of crossover imatinib therapy. The drug will continue to be provided by the Pharmaceutical Management Branch (PMB). See the information below about obtaining crossover drug.

4. Patients who completed treatment with placebo prior to April 1st, 2007 should discuss these results with their treating physician and decide whether therapy with imatinib is appropriate for them. These patients will **not** be eligible for imatinib provided by the PMB.

D. Obtaining crossover drug for patients who were receiving Placebo as of April 1st, 2007

1. Documentation of a patient's decision to receive crossover therapy must be provided on the Notification and Crossover Form. This form must be faxed directly to ACOSOG at (919) 668-7156 to ensure prompt processing of the patient's drug shipment.
2. **All crossover requests must be received by ACOSOG by 5:00pm EDT on July 13th, 2007.** Crossover requests received after 5:00pm EDT on July 13th, 2007 will not be eligible for imatinib provided by PMB.
3. ACOSOG will verify that the patient is eligible to receive crossover drug and will enter the information from the form into a web-based application, which will send an electronic drug request to the PMB.
4. The PMB will process the drug request and ship the Imatinib to the registering physician/site.

Section III: Common Patient Questions

Has Imatinib been approved by the FDA as postoperative adjuvant therapy following surgical resection?

No. Novartis will now work with ACOSOG investigators to file for regulatory approval.

How can I learn of additional results of the study?

The specific results of the study will be released to the scientific community and the public in the near future.

Will all patients who have a primary GIST removed now take 1 year of Imatinib?

Not necessarily. The final recommendations for patients with primary GIST who undergo complete surgical removal of their tumor will depend on the specific results of the study. Also, the study only tested patients with at least a 3 cm tumor.

Should I take Imatinib for more than 1 year after removal of my primary GIST?

This study only addressed the benefit of taking 1 year of therapy. Currently there are no data to answer whether Imatinib should be taken for longer than 1 year, but there are other ongoing studies addressing this question.

If I was taking Placebo, will I increase my risk of developing resistance to Imatinib if I now take 1 year of Imatinib therapy?

The answer to this question is unknown at the present time, but the general opinion of experts is that the benefits of taking Imatinib outweigh the risks.

Will my life be shorter if I was on the Placebo arm?

The trial was designed primarily to look for differences in recurrences. At this time, there is no difference in survival between patients taking Imatinib and those taking placebo. More information about survival differences may become available in the future as the study matures.

Section IV: Study Team Contact List

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