



AMERICAN COLLEGE OF SURGEONS ONCOLOGY GROUP

DEPARTMENT OF SURGERY
DUKE UNIVERSITY MEDICAL CENTER

CENTER FOR CLINICAL TRIALS
AND EVIDENCE BASED MEDICINE

July 14, 2004

Randomization Error in the ACOSOG Z9001 Clinical Study

The American College of Surgeons Oncology Group (ACOSOG) has detected a computer error that affected the randomization of some patients on the Z9001 clinical trial: "A Phase III randomized double-blind study of 400 mg of STI571 (Gleevec™) versus placebo in patients following resection of Gastrointestinal Stromal Tumor (GIST)." The error occurred between November 2003 and May 2004. As a result, sixty patients who entered the trial during that time were placed nonrandomly into the placebo arm, when approximately half of them should have been randomized to the treatment arm. Another 11 patients were randomized such that they had an 80 percent chance of receiving Gleevec™, when approximately half of them should have been randomized to the treatment arm. It is important to note that not all patients, who were registered to the Z9001 trial during the November 2003 to May 2004 time period, were affected by the randomization error. If you are one of the patients, who was affected by the randomization error, your doctor will be notifying you. Errors in randomization during clinical trials are rare and the present event involved only the ACOSOG Z9001 study. Other clinical trials in GIST have completely separate mechanisms of randomization and were not affected.

Once the error was identified, the ACOSOG Executive Committee developed a plan of action, which was based on discussions with the ACOSOG Data and Safety Monitoring Committee, the ACOSOG Ethics Committee and the Cancer Therapy Evaluation Program of the National Cancer Institute.

The physicians caring for the 60 patients assigned to placebo have been notified, personally and in writing. The 60 patients will be taken off the study because their assignment to the placebo arm became unblinded during the investigation of the randomization error. The 60 patients will meet individually with their physicians, who enrolled them on the study, to discuss available treatment options. It is important to understand that we currently do not know whether Gleevec™ is beneficial in patients who have undergone complete removal of a primary GIST. Indeed, this is why this clinical study is being performed. Therefore, patients who were placed in the placebo arm and did not receive Gleevec™, did receive the current standard of care, which is surgery plus observation.

The physicians caring for the 11 patients who had an 80 percent chance of receiving Gleevec™ have similarly been notified. Since the physicians do not know whether their patients are receiving placebo or Gleevec™, the 11 patients will be offered the option of staying on the study or withdrawing from the study. A patient who chooses to remain on the study will be required to sign a new consent form.

The US Food and Drug Administration, Novartis (the company who manufactures Gleevec™ and provides the drug for the Z9001 trial) and the Office of Human Research Protection have been notified of the randomization error.

Randomization Error in the ACOSOG Z9001 Clinical Study
July 14, 2004
Page 2

We have visited Mr. Norman Scherzer, the Executive Director of the Life Raft Group, and Dr. Mark Landesman, a member of the Science Committee of GIST Support International. They have been fully informed of the situation and our discussions have led to considerations of how ACOSOG can work with each of these support groups in the development and operation of future clinical studies involving patients with GIST.

The ACOSOG deeply regrets that this error has occurred. The Z9001 trial is a very important study. Appropriate randomization was restored, shortly after the randomization error was detected and equal assignment to placebo or GleevecTM has occurred since then. The length of the study will need to be extended by approximately three months. The ACOSOG has instituted measures to prevent the occurrence of such randomization errors in the future.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Samuel A. Wells, Jr.", written in a cursive style.

Samuel A. Wells, Jr., M.D.
ACOSOG Group Chair