

North Central Cancer Treatment Group

N0272: Phase I/II Trial of Imatinib Mesylate; (Gleevec; STI571) in Treatment of Recurrent Oligodendroglioma and Mixed Oligoastrocytoma

Addendum 7 – July 20, 2007

Summary

Scientific:

- Edition #6 dated June 28, 2006 of the investigator brochure for STI571 (imatinib, Gleevec) has been received. Therefore, the risk section of the consent forms has been revised accordingly.

Editorial:

- Administrative changes.

A replacement protocol is provided. Please replace your current copy with the one attached. Please keep this addendum with your protocol

Title page: S. Keith Anderson, M.S. replaces Yingwei Qi as the study statistician.

Now reflects the addition of Addendum 7 and revised NCI version date.

Protocol Resources

Page 2: The title for Vicki Bryhn has been updated to reflect “NCCTG *Research Base Protocol Administration Data Management Specialist*.”

Appendices IA, IB – Consent Forms

The risks for STI571 have been updated as follows due to the receipt of an updated version of the investigator brochure (IB):

Likely (events occurring greater than 20% of the time)(newly added due to IB review)

- Lowering of white blood cell counts leading to an increased risk of infections with or without fever
- Lowering of blood cells platelets that help to clot the blood (*wording change due to IB review*)
- **Lowering in a part of the red blood cells that carries oxygen in the body leading to an increased risk of anemia, which may require you to have a blood transfusion** (*moved from Less Likely due to IB review*)
- Fatigue (feeling tired, **lethargy, malaise**) (*expanded wording due to IB review*)
- Rash
- Muscle cramps and spasms, especially in your legs
- Nausea
- Vomiting
- Diarrhea
- **Pain of the abdomen** (*reworded and moved from Less Likely due to IB review*) **or head** (*in the CAEPR but not in the consent and now added due to IB review*)
- Swelling in your arms and legs
- Muscle pain
- Joint pain

Less Likely (*events occurring less than or equal to 20% of the time*) (*newly added due to IB review*)

- Allergic reactions
- ~~Lowering in a part of the red blood cells that carries oxygen in the body leading to an increased risk of anemia, which may require you to have a blood transfusion~~ (*moved to Likely due to IB review*)
- Build-up of fluid around your heart and/or infection in the lining around your heart
- ~~Fever~~ (*moved to “not known” due to IB review*)
- Chills and aches
- Increased sweating
- Weight gain **or weight loss** (*additional wording new due to IB review*)
- Hair loss or thinning
- Darkening or lightening of the skin
- Itching
- Severe skin reaction that may include rash, shedding, or death of skin tissue and could cause you to be hospitalized for treatment
- Loss of appetite
- **Ascites** (build up of fluid in the stomach) (*expanded wording due to IB review*)
- Constipation
- Loss of body fluids (dehydration – which may require fluids into a vein)
- **Flatulence** (gas) (*expanded wording due to IB review*)
- Heartburn **or indigestion** (*expanded wording due to IB review*)
- Ulcers in the mouth (**mucositis**), esophagus, stomach or small bowel (*expanded wording due to IB review*)
- **Dysgeusia** (change in how things taste) (*expanded wording due to IB review*)
- Hemorrhage/bleeding (in your brain, spinal fluid, GI tract, tumor, urine, etc.)
- Swelling of the head and neck area
- ~~Abnormal increases in~~ liver or kidney blood tests **and/or kidney failure**. Your blood will be checked regularly to see if this has happened (*wording change due to IB review*)
- Laboratory abnormalities such as disturbances in electrolyte balance (chemicals found in the blood, i.e., sodium, potassium, phosphates, **calcium**) (*wording change due to IB review*)
- Arthritis/**joint swelling** (damage to your joints) (*wording change due to IB review*)
- Injury to your bones (**osteonecrosis**) (*wording change due to IB review*)
- Dizziness
- Abnormal change in brain function **like confusion and altered consciousness (encephalopathy) and abnormal buildup of cerebrospinal fluid in the ventricles of the brain (hydrocephalus)** (*events were in the CAEPR but not in the consents and now added due to IB review*)
- ~~Build up of fluid in the brain~~ (*included in the event above*)
- Mood changes, **depression** (*newly added due to IB review*)
- Weakness
- **Nerve problems, like numbness or tingling of your hands or feet (neuropathy) or swelling around the optic nerve (optic disc edema)** (*rewording due to IB review*)
- ~~Swelling of the nerve in the back of the eye~~ (*included in the event above*)
- Increased tear production in your eyes
- Pain in the ~~stomach~~ (*moved to Likely due to IB review*), back, chest, and throat
- Headache
- Cough
- Difficulty breathing
- Swelling and build-up of fluid in your lungs
- Kidney damage/failure

- Flu-like symptoms
- Blood clots, including clots that may travel to the lung and cause breathing problems
- ~~Liver damage. This has happened in a few patients taking other medicines at the same time as their imatinib. These other medicines may cause liver damage when taken with imatinib and include acetaminophen (Tylenol[®]). You should tell your doctor about any other medicines you may be taking while on imatinib, including over the counter medicines you can get without a prescription, even if you only take them every once in a while. You should not take more than 500 mg of acetaminophen at a time, and follow the instructions on the package label. (moved to “not known” due to IB review)~~
- ~~Inability to sleep (moved to “not known” due to IB review)~~
- Nose bleeds
- Dry mouth
- Night sweats
- Sore throat or build-up of fluid in your throat tissues
- **Infection** (newly added due to IB review)
- **Shortness of breath** (newly added due to IB review)
- **Pain** (newly added due to IB review)

Rare but Serious (events occurring less than 2-3% of the time) (newly added due to IB review)

(These side effects may or may not be related to imatinib but may occur during treatment)

- Decrease in the heart's ability to pump blood
- Heart problems (heart failure, ~~heart attacks~~ (moved to “not known” due to IB review), fast heart rate)
- Bruising or redness of the white part of the eyes
- Dry eyes
- Inflammation of the small bowel, pancreas and/or gallbladder
- Blockage of the bowel
- Jaundice
- Relapse of the hepatitis virus (if you have had hepatitis C in the past)
- Cold sores on your lip
- Shingles
- Changes in your blood pressure
- Pneumonia
- Inflammation of your lung(s)
- Increase in appetite
- Swelling of your joints
- Pain down your leg (sciatica)
- A condition where the tumor dies too fast, causing toxic substances to be released into your blood, which may make you sick and possibly require hospitalization
- Fainting
- Depression
- Difficulty urinating
- Breast enlargement
- Breakage of the nails
- Skin rash that is worse when you are exposed to sunlight
- Flushing
- A harsh, creaking sound from the voice box

~~Interaction between imatinib and anti-seizure medicines:~~

~~Imatinib may interact with certain anti-seizure and other medicines that you are taking. Your doctor will need to check for this and adjust your seizure medicines while you are receiving imatinib. There is a chance that the blood levels of your anti-seizure medicine will be lowered while you are on treatment with imatinib. This could cause occasional or frequent seizure if your anti-seizure dosage is not adjusted while taking the imatinib. You should tell your doctor if you are currently taking any anti-seizure medicines.~~ (moved to “not known” due to IB review)

Tumors in the urinary system or reproductive organs have also been reported in animals.

The following side effects have been reported for patients taking part in other STI571 research studies. It is not known if these side effects were related to the STI571: (this section is newly added due to IB review)

- **Autoimmune reactions including vasculitis** (newly added due to IB review)
- **Heart attack** (moved from Rare but serious due to IB review) **or death** newly added due to IB review)
- **Abnormal blood clotting or bleeding (disseminated intravascular coagulation)** (newly added due to IB review)
- **Inability to sleep** (moved from Less Likely due to IB review)
- **Dry skin** (newly added due to IB review)
- **Stomach and intestinal problems, like perforation, irritation** (newly added due to IB review)
- **Imatinib may interact with certain anti-seizure and other medicines that you are taking. Your doctor will need to check for this and adjust your seizure medicines while you are receiving imatinib. There is a chance that the blood levels of your anti-seizure medicine will be lowered while you are on treatment with imatinib. This could cause occasional or frequent seizure if your anti-seizure dosage is not adjusted while taking the imatinib. You should tell your doctor if you are currently taking any anti-seizure medicines.** (moved from Rare but serious due to IB review)
- **Liver damage. This has happened in a few patients taking other medicines at the same time as their imatinib. These other medicines may cause liver damage when taken with imatinib and include acetaminophen (Tylenol®). You should tell your doctor about any other medicines you may be taking while on imatinib, including over the counter medicines you can get without a prescription, even if you only take them every once in a while. You should not take more than 500 mg of acetaminophen at a time, and follow the instructions on the package label.** (moved from Rare but serious due to IB review)
- **Fever** (moved from Less Likely due to IB review)
- **Abnormal pancreas tests** (newly added due to IB review)
- **Kidney stones** (newly added due to IB review)
- **Rare neurological condition called Guillain Barre syndrome, which is an autoimmune problem characterized by severe nerve weakness** (newly added due to IB review)
- **Blurred vision and other eye problems** (newly added due to IB review)

NOTE: STI571 in combination with other agents could cause an exacerbation of any adverse event currently known to be caused by the other agent, or the combination may result in events never previously associated with either agent. (newly added due to IB review)