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Gleevec Treatment for (CML)

For most patients with chronic myelogenous leukemia (CML) in chronic phase, a drug called Gleevec (also known as imatinib mesylate) is the standard first treatment. Described below are some details about Gleevec as a treatment for CML.

Measuring Responses to Gleevec

Patients with CML have an abnormal chromosome called the Philadelphia chromosome. The Philadelphia chromosome creates an enzyme called tyrosine kinase. This enzyme signals the body to make too many white blood cells. Gleevec works by blocking the tyrosine kinase enzyme so that the body stops (or slows down) making too many white blood cells. Doctors measure how well Gleevec is working by looking at three responses:

- **Hematologic** (blood) response – how well the blood counts return to normal.
- **Cytogenetic** (cellular) response – the number of cells with the Philadelphia chromosome. A sample of 20 to 30 cells are checked. A major response means at least 66% of cells are normal, and a complete response means all cells tested are normal.
- **Molecular** response – molecular testing can find as few as one cell in a million with the Philadelphia chromosome. This test may be called a BCR/ABL by PCR test (PCR stands for polymerase chain reaction). This is because the test looks for the BCR/ABL translocation, which is a marker of the Philadelphia chromosome.

If even a small number of cells with the Philadelphia chromosome remain in the body, the CML could return. Therefore, the goal of treatment is to achieve a complete molecular response.

Results of Clinical Trials of Gleevec

A clinical trial is a research study meant to help improve current treatments or obtain information on new treatments. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment. Beginning in 2000, a large clinical trial was done to compare Gleevec to interferon plus cytarabine – the best standard chemotherapy treatment at the time [1]. The study included 1,106 patients with chronic phase CML who were assigned at random to be treated either with Gleevec or with interferon and cytarabine. The estimated rates of response an average of 18 months after patients began treatment are shown in the table below.

Type of Response	Patients treated with Gleevec who responded	Patients Treated with Interferon and Cytarabine who Responded
Completed hematologic (blood response)	96.8%	69%
Major cytogenetic (cellular) response	87.1%	34.7%
Completed cytogenetic (cellular) response	76.2%	14.5%
Major molecular response	39% (after 12 months)	2% (after 12 months)
Disease did not get worse	96.7%	91.5%

In addition, the patients taking Gleevec had fewer side effects than those taking interferon and cytarabine. More time must pass before doctors know whether the patients in this study continue to do well on Gleevec over the long term.

If even a small number of cells with the Philadelphia chromosome remain in the body, the CML could return. One way doctors are trying to get rid of these cells is by giving higher doses of Gleevec. In one clinical trial, 114 patients newly diagnosed with CML were given twice the usual dose of Gleevec (400 mg twice a day) [2]. An average of 15 months after starting treatment:

- 63% of the patients showed a major molecular response.
- None of the patients had their disease worsen to accelerated or blast phase.

Questions about Gleevec

Because Gleevec is fairly new, there are still questions about it, including:

- How good does a patient's response need to be to control the disease? Many patients show only a partial response.
- How long will Gleevec control CML?
- Does Gleevec actually cure patients with CML? Can patients with no sign of disease eventually stop taking Gleevec?
- What is the best treatment for patients who do not respond to Gleevec?

Gleevec does not work as well for patients in accelerated phase or blast phase. Also, some patients in chronic phase do not respond to Gleevec or can lose their response over time (develop resistance). Doctors are looking for new ways to help these patients. Some options include using a marrow or peripheral (circulating) blood cell transplant, giving higher doses of Gleevec and combining Gleevec with other drugs.

Researchers are also building on what they learned with Gleevec to develop new drugs. These drugs have to be tested in clinical trials before doctors will know whether they work. For example, the second generation of Gleevec (known as BMS-354825) is now being tested in early clinical trials for patients who do not respond to Gleevec.

References

O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med. 2003; 348(11):994-1004. http://content.nejm.org/cgi/content/abstract/348/11/994?view=abstractpmid=12637609

Kantarjian H, Talpaz M, O'Brien S, et al. High-dose imatinib mesylate therapy in newly diagnosed Philadelphia chromosome-positive chronic phase chronic myeloid leukemia. Blood. 2004; 103(8):2873-2878. http://www.bloodjournal.org/cgi/content/abstract/103/8/2873

The NMDP's Office of Patient Advocacy (OPA) continually develops resources and materials to help patients, family members and doctors with questions about marrow or cord blood transplantation. In addition to print, audio and visual materials, OPA has bilingual (Spanish/English) case managers and LanguageLine interpreter services available for callers. All OPA materials and services are free and confidential. Call the OPA toll-free at 1 (888) 999-6743. Outside the United States call (612) 627-8140, or visit marrow.org/patient