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New data show Glivec® halts progression to advanced stages of life-threatening form of leukemia in sixth year of treatment

- *Risk of disease progression continues to drop from the second year of treatment; no patients taking Glivec in sixth year progressed from initial disease phase*
- *Long-term survival trend may suggest many patients could approach normal life expectancy with continued treatment*

Basel, December 9, 2007 – New data from the largest clinical trial in newly diagnosed patients with a life-threatening form of leukemia showed that long-term use of Glivec® (imatinib)* can halt progression to advanced disease stages in the sixth year of treatment.

Results of the International Randomized Interferon versus STI571 (IRIS) study reveal that after two years of treatment, the rate of disease progression continued to decline and fell to 0% in the study's sixth year. In addition, the estimated overall six-year survival rate for patients treated with Glivec was 88%.

Lead investigators presented the latest findings from this landmark study involving more than 1,100 newly diagnosed patients with a form of the disease known as Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) at the 49th Annual Meeting of the American Society of Hematology (ASH).

Patients in the initial (chronic) phase of CML who received continuous treatment with Glivec did not progress to advanced stages of the disease. Without treatment, CML typically progresses over three to five years from the initial phase through a transition (accelerated) phase to a rapidly fatal form called blast crisis¹.

“If this survival trend continues, many patients with CML may approach normal life expectancy with continued Glivec treatment,” said Dr. Brian Druker, MD, Director of the Oregon Health & Science University Cancer Institute Center; the JELD-WEN Chair of Leukemia Research, Howard Hughes Medical Institute Investigator and a member of the National Academy of Sciences.

Most CML patients are in the chronic phase when the disease is diagnosed. Before Glivec was available, about 50% of patients with Ph+ CML progressed from the initial phase to more advanced stages after only three to five years². Once patients reached the final blast crisis phase, survival was generally three to six months³.

With a unique six-year record of safety and efficacy, Glivec remains the first-line drug therapy for all patients with Ph+ CML.

* Known as Gleevec® (imatinib mesylate) tablets in the US, Canada and Israel.

Glivec has continued to be generally well tolerated as initial drug therapy for Ph+ CML in chronic phase. At the six-year follow-up, the type and frequency of adverse events were similar to previously reported profiles. Newly occurring or worsening grade 3 or 4 hematologic or biochemical adverse events were infrequent.

IRIS is an open-label Phase III clinical trial enrolling 1,106 newly diagnosed patients with Ph+ CML in chronic phase in 177 centers across 16 countries. There are two arms to the study: one group of patients received Glivec 400 mg per day, while the other received a target dose of interferon (IFN) of 5 MIU/m²/day in combination with cytarabine (Ara-C) 20 mg/m²/day for 10 days each month. Because of tolerability issues, lack of response or loss of response, 65% of patients in the IFN/Ara-C arm crossed over to the Glivec arm, whereas only 3% of patients in the Glivec arm crossed over to the IFN/Ara-C arm¹.

Cumulative best responses to Glivec treatment improved dramatically between the first and sixth years of treatment. Over the period, the number of Glivec-treated patients showing complete cytogenetic response (or elimination of the abnormal Philadelphia chromosome associated with CML) rose from 70% in the first year to 87% by the sixth year of treatment.

The estimated overall survival rate for patients receiving Glivec was 88% when considering deaths from all causes. When deaths from causes unrelated to CML or following transplantation are excluded, the estimated overall survival rate was 95%¹. Less than 5% of patients died of CML¹.

The rate of disease progression continued to decline in the sixth year of the study, with a 0.4% event rate (including loss of response) and a 0% rate of progression to advanced disease between years five and six among patients who remained on Glivec after five years.

No new serious safety issues were identified between the fifth and sixth year of treatment¹.

In a separate study published last month in the ASH journal *Blood*, Glivec produced a high six-year estimated overall survival rate (76%) in chronic-phase CML patients who had previously failed treatment with interferon. Most of these high-risk patients (57%) also achieved the best treatment outcome – a complete cytogenetic response – and many (40%) were still in cytogenetic response after six years of treatment with Glivec⁴.

About Glivec

Glivec is approved in more than 90 countries including the US, EU and Japan for the treatment of all phases of Ph+ CML. Glivec is also approved in the EU, US and other countries for the treatment of patients with Kit (CD117)-positive gastrointestinal tumors (GIST), which cannot be surgically removed and/or have already spread to other parts of the body (metastasized). In Japan, Glivec is approved for the treatment of patients with Kit (CD117)-positive GIST. In the EU, Glivec is also approved for the treatment of adult patients with newly diagnosed Ph+ acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy and as a single agent for patients with relapsed or refractory Ph+ ALL. Glivec is also approved for the treatment of adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP) who are not eligible for surgery. Glivec is also approved for the treatment of patients with myelodysplastic/myeloproliferative diseases (MDS/MPD). Glivec is also approved for hypereosinophilic syndrome and/or chronic eosinophilic leukemia (HES/CEL).

The effectiveness of Glivec is based on overall hematologic and cytogenetic response rates and progression-free survival in CML, on hematological and cytogenetic response rates in Ph+ ALL, and on objective response rates in GIST and DFSP. There are no controlled trials demonstrating increased survival. Not all indications are available in every country.

Glivec contraindications, warnings and adverse events

The majority of patients treated with Glivec in clinical trials experienced adverse events at some time. Most events were of mild to moderate grade and treatment discontinuation was not necessary in the majority of cases.

The safety profile of Glivec was similar in all indications. The most common side effects included nausea, superficial edema, muscle cramps, skin rash, vomiting, diarrhea, abdominal pain, myalgia, arthralgia, hemorrhage, fatigue, headache, joint pain, cough, dizziness, dyspepsia and dyspnea, dermatitis, eczema, fluid retention, as well as neutropenia, thrombocytopenia and anemia. Glivec was generally well-tolerated in all of the studies that were performed, either as monotherapy or in combination with chemotherapy, with the exception of a transient liver toxicity in the form of transaminase elevation and hyperbilirubinemia observed when Glivec was combined with high dose chemotherapy.

Rare/serious adverse reactions include: sepsis, pneumonia, depression, convulsions, cardiac failure, thrombosis/embolism, ileus, pancreatitis, hepatic failure, exfoliative dermatitis, angioedema, Stevens-Johnson syndrome, renal failure, fluid retention, edema (including brain, eye, pericardium, abdomen and lung), hemorrhage (including brain, eye, kidney and gastrointestinal tract), diverticulitis, gastrointestinal perforation, tumor hemorrhage/necrosis, hip osteonecrosis/avascular necrosis.

Patients with cardiac disease or risk factors for cardiac failure should be monitored carefully and any patient with signs or symptoms consistent with cardiac failure should be evaluated and treated. Cardiac screening should be considered in patients with HES/CEL, and patients with MDS/MPD with high level of eosinophils (echocardiogram, serum troponin level).

Glivec is contraindicated in patients with known hypersensitivity to imatinib or any of its excipients. Women of childbearing potential should be advised to avoid becoming pregnant while taking Glivec.

Disclaimer

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