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MEDIA RELEASE · COMMUNIQUE AUX MEDIAS · MEDIENMITTEILUNG

Data prove Glivec® is superior treatment for patients newly diagnosed with chronic myeloid leukemia

Nearly three-quarters of patients achieve major treatment goal in study comparing Glivec with traditional therapy; Glivec also significantly delays disease progression

Basel, 13 March 2003 — Glivec® (imatinib)* should be considered the first drug treatment option for patients with newly diagnosed chronic myeloid leukemia (CML), according to data published in the 13 March 2003 issue of the *New England Journal of Medicine* (*NEJM*). They confirm that newly diagnosed patients in the chronic phase of CML are substantially more likely to achieve a complete cytogenetic response, a major goal of treatment, when treated first with Glivec than with the traditional combination therapy, interferon and cytosine arabinoside (IFN/Ara-C). In addition, the data show that Glivec significantly delays the progression of the disease to advanced stages. The data represent 18 months of follow-up from the International Randomized Study of Interferon vs. STI571 (IRIS), the first head-to-head study comparing Glivec with IFN/Ara-C.

"As we look at the benefits of Glivec over a longer period of time, the results continue to be very impressive," said Dr. Stephen G. O'Brien, lead investigator, Department of Hematology, University of Newcastle Medical School, United Kingdom. "By all parameters measured in the IRIS study, early use of Glivec yielded superior results compared to interferon/Ara-C. It is still too early to be sure of long-term outcomes in Glivec-treated patients, but from the results we have seen to date, there is reason for optimism."

Study Details

The study was conducted in 1 106 patients. At the 18-month follow-up after the last patient was recruited, 74% of newly diagnosed patients treated with Glivec, taken orally at 400 mg daily, had achieved a complete cytogenetic response, compared with 8% of those treated with IFN/Ara-C ($P<0.001$).** A major cytogenetic response was achieved by 85% of patients taking Glivec compared with 22% of patients treated with IFN/Ara-C ($P<0.001$). A complete cytogenetic response means that no cells containing the Philadelphia chromosome (Ph+), the genetic abnormality that characterizes most cases of CML, are detected; a major cytogenetic response is defined as the detection of less than 35% Ph+ cells remaining. Patients taking Glivec also had an improved overall progression-free survival compared with those taking IFN/Ara-C (at 18 months: 92% vs. 74%, respectively; $P<0.001$). A decrease in the progression to more advanced stages of disease (accelerated or blast crisis) with Glivec was also achieved.

Only 2% of patients in the Glivec arm crossed over to the IFN/Ara-C arm, whereas 58% of patients in the IFN/Ara-C arm crossed over to the Glivec arm because of tolerability reasons or lack or loss of response to treatment. Another 12% of patients in the Glivec arm withdrew from the study, compared with 32% of patients in the IFN/Ara-C arm. Severe side effects were much more common in the IFN/Ara-C arm, consistent with the high turnover rate due to intolerance.

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* In the US: Gleevec™ (imatinib mesylate)

** Based on observed response rate. Estimated rates by Kaplan-Meier analysis demonstrated 76% vs. 14% respectively.

These 18-month data were originally presented in December 2002 at the plenary session of the annual meeting of the American Society of Hematology (ASH) in Philadelphia, Pennsylvania, USA.

Glivec
Glivec is indicated for first-line treatment of adult patients with Ph+ CML in the EU, US and Japan and a number of other markets. Marketing approval in the EU, Switzerland and other countries includes the treatment of pediatric patients. In addition, Glivec is already approved in over 80 countries for the treatment of adult patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

Glivec is also approved in the EU, US and more than 45 other countries for the treatment of patients with Kit (CD 117)-positive unresectable (inoperable) and/or metastatic malignant gastrointestinal stromal tumors (GISTs).

Contraindications and Adverse Events
In the first-line study (IRIS), the safety profile with Glivec was similar to that of previous Phase II studies in other CML patients. The majority of patients treated with Glivec experienced adverse events at some time. Most events were of mild to moderate grade and treatment was discontinued for adverse events only in 2% of patients in chronic phase, 3% in accelerated phase and 5% in blast crisis. The most common side effects included nausea, superficial edema, muscle cramps, skin rash, vomiting, diarrhea, hemorrhage, fatigue, headache, joint pain, cough, dizziness, dyspepsia and dyspnea, as well as neutropenia and thrombocytopenia.

The foregoing release contains forward-looking statements that can be identified by terminology such as “prove,” “should be considered,” “superior,” “significantly,” “substantially,” “more likely,” “optimism,” “very impressive,” or similar expressions, or by discussions regarding potential new indications for Glivec, or regarding the long-term impact of a patient's use of Glivec. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Glivec to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Glivec will be approved for any additional indications in any market. Neither can there be any guarantee regarding the long-term impact of a patient's use of Glivec. In particular, management's ability to ensure satisfaction of the health authorities' further requirements is not guaranteed and management's expectations regarding commercialization of Glivec could be affected by, among other things, additional analysis of Glivec clinical data; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; and other risks and factors referred to in the Company's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected.

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2002, the Group's businesses achieved sales of CHF 32.4 billion (USD 20.9 billion) and a net income of CHF 7.3 billion (USD 4.7 billion). The Group invested approximately CHF 4.3 billion (USD 2.8 billion) in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 72 900 people and operate in over 140 countries around the world. For further information please consult http://www.novartis.com.

Additional information on Novartis Oncology and Glivec can be found at www.novartisoncology.com or www.glivec.com. Additional media information can be found at www.novartisoncologyvpo.com.

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