

EXTEND RECURRENCE-FREE SURVIVAL WITH LONGER ADJUVANT GLIVEC THERAPY*

Recurrence rates increase after treatment interruption

Discontinuation of therapy removes the therapeutic benefit of KIT inhibition

Several studies show extending therapy beyond 1 year improves recurrence-free survival

NCCN guidelines recommend at least 1 year of adjuvant GLIVEC, but longer treatment may be justified in patients at higher risk



*Individual patients' results may vary.

GLIVEC® (imatinib) is indicated for the treatment of adult patients with KIT (CD117)-positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST) and for the adjuvant treatment of adult patients who are at significant risk of relapse following resection of KIT (CD117)-positive GIST. Patients who have a low or very low risk of recurrence should not receive adjuvant treatment.

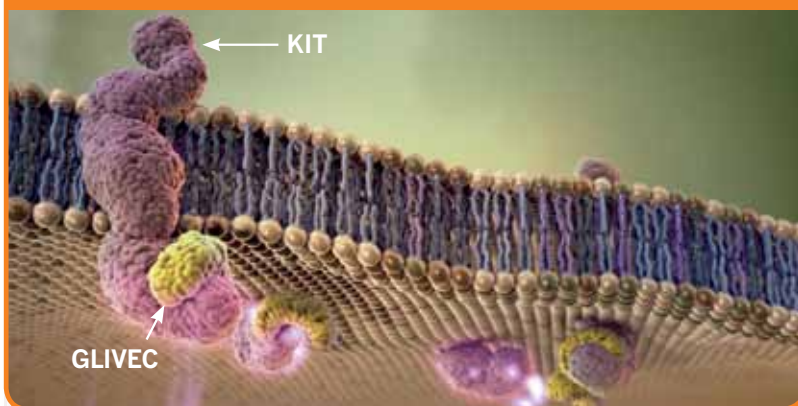
 **glivec**[®]
imatinib



Continuous KIT suppression with GLIVEC may prolong recurrence-free survival¹

- Adjuvant treatment with GLIVEC resulted in 98% recurrence-free survival (RFS) at 1 year across all risk groups versus placebo²
- The rate of recurrence increased around 6 months after discontinuing GLIVEC therapy at 1 year, suggesting the importance of continuous KIT suppression²

Removal of GLIVEC means KIT activation can continue uncontrolled¹



NCCN* recommends at least 12 months of GLIVEC therapy following resection³

- Adjuvant GLIVEC for at least 12 months is recommended for patients at intermediate or high risk
- Optimal treatment duration has not yet been determined
- Patients at high risk may justify a longer course of GLIVEC therapy

*United States National Comprehensive Cancer Network.

References: 1. DeVita VT Jr, Hellman S, Rosenberg SA. *Cancer: Principles & Practice of Oncology*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005. 2. DeMatteo RP, Ballman KV, Antonescu CR, et al; for the American College of Surgeons Oncology Group (ACOSOG) Intergroup Adjuvant GIST Study Team. Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double-blind, placebo-controlled trial. *Lancet*. 2009;373(9669):1097-1104. 3. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (Version 2.2009). ©2009 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed December 21, 2009. To view the most recent and complete version of the guideline, go online to www.nccn.org.

Maintaining GLIVEC beyond 1 year improves recurrence-free survival^{4,5}

- Longer treatment duration improves recurrence-free survival (RFS) in high-risk patients^{2,6}

RFS across HIGH-RISK groups

	Duration of therapy (GLIVEC)		
	1-year treatment	2-year treatment	
	(DeMatteo et al, 2009) ^{2,6,a,b}	(Kang et al, 2008) ^{4,c,d}	(Li et al, 2009) ^{5,e}
1-year RFS	95%	98%	100%
2-year RFS	81%	93%	92%
RFS points lost at 2 years	14	5	8

 = patient on therapy at time of measurement

- a. A randomized, multicenter, phase 3 clinical study in which patients (N=713) were randomized to receive GLIVEC 400 mg/day (n=359) or placebo (n=354) for 1 year following surgery. Both 1- and 2-year RFS rates are shown for patients who had completed the treatment (or placebo) for the course of study, which was 1 year. One- and 2-year RFS rates for placebo were 64% and 47%, respectively.
- b. Subanalysis comprised patients at high risk (according to United States National Institutes of Health) from a randomized, multicenter, phase 3 clinical study in which patients (n=179) were randomized to receive GLIVEC 400 mg/day (n=93) or placebo (n=86) for 1 year following surgery.
- c. A phase 2 multicenter clinical study in which patients (N=47) at high risk of recurrence received GLIVEC 400 mg/day for up to 2 years following surgery.
- d. High risk was defined as patients with all of the following criteria: primary localized GIST with large size, high mitotic count, and *KIT* exon 11 mutation.
- e. A phase 2 single-center clinical study in which patients (N=105) at high or intermediate risk of recurrence were randomized to receive GLIVEC 400 mg/day or follow-up alone for up to 3 years following surgery. One- and 2-year RFS rates for the control group were 82% and 46%, respectively.

Use of these data is subject to local rules and regulations.

References: 2. DeMatteo RP, Ballman KV, Antonescu CR, et al; for the American College of Surgeons Oncology Group (ACOSOG) Intergroup Adjuvant GIST Study Team. Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double-blind, placebo-controlled trial. *Lancet*. 2009;373(9669):1097-1104. 4. Kang B, Lee J, Ryu M, et al. A phase II study of imatinib mesylate as adjuvant treatment for curatively resected high-risk localized gastrointestinal stromal tumors. *J Clin Oncol*. 2009;27(suppl). ASCO abstract e21515. 5. Li J, Gong J, Li J, Wu A, Shen L. Adjuvant therapy with imatinib in gastrointestinal stromal tumor patients with intermediate or high risk: interim analysis from a single-centre contrast study. Poster presented at: 45th Annual Meeting of the American Society of Clinical Oncology; May 29-June 2, 2009; Orlando, FL. Poster 10556. 6. GLIVEC® (imatinib) Summary of Product Characteristics. Basel, Switzerland: Novartis Pharma AG; May 2010.

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Important Safety Information

Contraindications: Hypersensitivity to imatinib or to any of the excipients.

Special warnings and precautions

Precautions/Warnings: GLIVEC should be taken with food and a large glass of water to minimize the risk of gastrointestinal disturbances. Severe fluid retention has occurred. It is recommended that patients be weighed regularly and undergo regular monitoring of complete blood counts and liver function tests. Caution should be exercised in patients with history of cardiac disease. Carefully monitor patients with cardiac impairment or risk factors for cardiac failure. Caution should be exercised in patients with severe renal disease. Monitor TSH levels in thyroidectomy patients undergoing levothyroxine replacement. GLIVEC should not be used during pregnancy unless clearly necessary. GLIVEC should not be used by breast-feeding mothers.

Interactions: Caution should be exercised with CYP3A4 inhibitors (eg, ketoconazole, clarithromycin), which may increase plasma concentrations of imatinib. Caution should be exercised with CYP3A4 inducers (eg, dexamethasone, rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort), which may decrease plasma concentrations of imatinib. Caution should be exercised with substrates of CYP3A4 (eg, triazolo-benzodiazepines, dihydropyridine calcium channel blockers, simvastatin, cyclosporin, pimozide), CYP2C9 (eg, warfarin) or CYP2D6 (eg, metoprolol). Caution should be exercised with concomitant use of paracetamol/acetaminophen.

Adverse reactions

Very common (>1/10): Weight increase, neutropenia, thrombocytopenia, anemia, headache, nausea, diarrhea, vomiting, dyspepsia, abdominal pain, periorbital edema, dermatitis, eczema, rash, muscle spasm and cramps, musculoskeletal pain including myalgia, arthralgia, bone pain, fluid retention and edema, fatigue.

Common (>1/100, ≤1/10): Weight decrease, pancytopenia, febrile neutropenia, dizziness, paresthesia, taste disturbance, hypoesthesia, eyelid edema, lacrimation increase, conjunctival hemorrhage, conjunctivitis, dry eye, blurred vision, dyspnea, epistaxis, cough, flatulence, abdominal distension, gastroesophageal reflux, constipation, dry mouth, gastritis, GI bleeding, pruritus, facial edema, dry skin, erythema, alopecia, night sweats, photosensitivity reaction, joint swelling, anorexia, flushing, hemorrhage, weakness, pyrexia, anasarca, chills, rigors, increased hepatic enzymes, insomnia.

Note: Before prescribing, please read full Summary of Product Characteristics.