

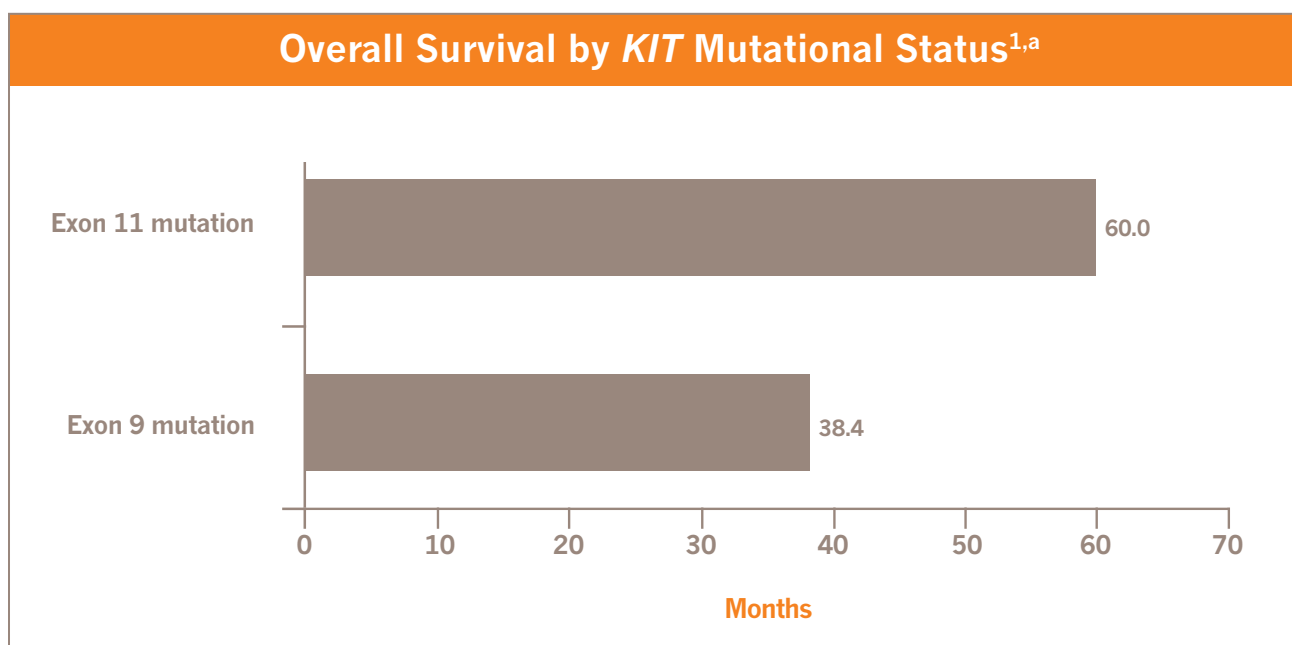
IF YOU SUSPECT A

***KIT* EXON 9 MUTATION**

GLIVEC 400 MG MAY NOT BE ENOUGH

***KIT* exon 9 mutations are challenging to treat¹**

- Patients with *KIT* exon 9 mutations have a poor prognosis
 - An analysis of 397 patients with unresectable/metastatic *KIT*+ GIST demonstrated that the overall survival of patients with *KIT* exon 9 mutations was significantly shorter than those with exon 11 mutations ($P=0.011$)



^aPatients receiving GLIVEC 400 mg or 800 mg.

GLIVEC[®] (imatinib) is indicated for the treatment of adult patients with *KIT* (CD117)-positive unresectable and/or metastatic, malignant gastrointestinal stromal tumors (GIST).

Please see Important Safety Information on back panel and enclosed Summary of Product Characteristics.



glivec[®]
imatinib



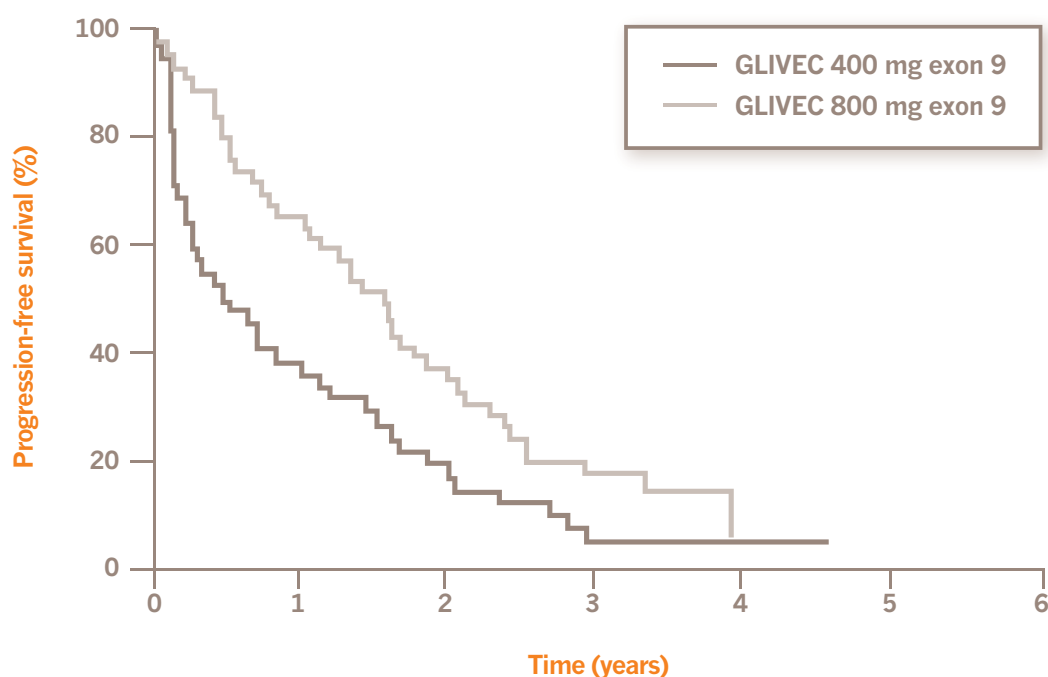
GLIVEC 800 MG

PROVIDES SIGNIFICANT BENEFITS FOR PATIENTS WITH *KIT* EXON 9 MUTATIONS²

GLIVEC 800 mg extends progression-free survival²

- In a meta-analysis with a median follow-up of 45 months, among patients with *KIT* exon 9 mutations, those treated with GLIVEC 800 mg/day had significantly longer progression-free survival than those treated with GLIVEC 400 mg/day ($P=0.017$)

Progression-free Survival by GLIVEC Dosage²



No. of patients at risk:

	O	N	0	1	2	3	4	5
400 mg exon 9:	40	42	16	8	2	1	0	0
800 mg exon 9:	42	49	32	16	8	0	0	0

O=events.
N=number of patients.

GLIVEC 800 mg increases response rate and reduces risk²

- 47% of patients with *KIT* exon 9 mutations treated with GLIVEC 800 mg/day achieved best overall response vs 21% of patients treated with GLIVEC 400 mg/day ($P=0.0037$)
- Risk of progression or death decreased by 42% for patients with *KIT* exon 9 mutations treated with GLIVEC 800 mg/day vs those treated with GLIVEC 400 mg/day ($P=0.017$)
- GLIVEC 800 mg may show potential as neoadjuvant treatment for patients with locally advanced disease and *KIT* exon 9 mutations to decrease tumor burden before surgery

ESMO and NCCN recommend GLIVEC 800 mg/day for patients with *KIT* exon 9 mutations^{3,4}

- ESMO guidelines designate GLIVEC 800 mg/day as the standard treatment for patients with *KIT* exon 9 mutations³
- NCCN guidelines state that patients with documented *KIT* exon 9 mutations may benefit from GLIVEC 800 mg/day⁴
- Data on patients with *KIT* exon 9 mutations resulted in the first major incorporation of mutation status into the treatment decision-making process

Suspect a *KIT* exon 9 mutation if:

- The tumor is located in the small bowel
— 95% of tumors with *KIT* exon 9 mutations are in the small bowel⁵

ESMO=European Society for Medical Oncology.
NCCN=National Comprehensive Cancer Network.

References: 1. Heinrich MC, Owzar K, Corless CL, et al. Correlation of kinase genotype and clinical outcome in the North American intergroup phase III trial of imatinib mesylate for treatment of advanced gastrointestinal stromal tumor: CALGB 150105 study by Cancer and Leukemia Group B and Southwest Oncology Group. *J Clin Oncol.* 2008;26(33):5360-5367. 2. Van Glabbeke M; on behalf of the Gastrointestinal Stromal Tumor Meta-Analysis Group (MetaGIST). Comparison of two doses of imatinib for the treatment of unresectable or metastatic gastrointestinal stromal tumors: a meta-analysis of 1,640 patients. *J Clin Oncol.* 2010;28(7):1247-1253. 3. Casali PG, Jost L, Reichardt P, Schlemmer M, Blay J-Y; on behalf of the ESMO Guidelines Working Group. Gastrointestinal stromal tumours: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol.* 2009;20(suppl 4):iv64-iv67. 4. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (Version 1.2010). ©2010 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed April 9, 2010. To view the most recent and complete version of the guidelines, go online to www.nccn.org. 5. Corless CL, Fletcher JA, Heinrich MC. Biology of gastrointestinal stromal tumors. *J Clin Oncol.* 2004;22(18):3813-3825.



glivec[®]
imatinib



GLIVEC® (imatinib) is indicated for the treatment of adult patients with KIT (CD117)-positive unresectable and/or metastatic, malignant gastrointestinal stromal tumors (GIST).

Important Safety Information

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

Precautions/Warnings: Should be taken with food and a large glass of water to minimize the risk of gastrointestinal disturbances. Beware of severe fluid retention. It is recommended that patients be weighed regularly. Regular monitoring of complete blood counts and liver function tests. Caution in patients with history of cardiac disease. Careful monitoring of patients with cardiac disease or risk factors for cardiac failure. Monitoring of TSH levels in thyroidectomy patients undergoing levothyroxine replacement. Should not be used during pregnancy unless clearly necessary. Should not be used by breast-feeding mothers.

Interactions: Caution with CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin). Caution with CYP3A4 inducers (e.g. dexamethasone, rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort). Caution with substrates of CYP3A4 (e.g. triazolo-benzodiazepines, dihydropyridine calcium channel blockers, simvastatin, cyclosporin, pimozone), CYP2C9 (e.g. warfarin) or CYP2D6 (e.g. metoprolol). Caution with concomitant use of paracetamol/acetaminophen.

Adverse reactions:

Very common: headache, nausea, vomiting, diarrhea, dyspepsia, abdominal pain, myalgia, arthralgia, muscle spasm or cramps, bone pain, dermatitis, eczema, rash, fatigue, weight increase.

Common: anorexia, insomnia, dizziness, paresthesia, taste disturbance, hypoesthesia, flushing, photosensitivity reaction, weakness, pyrexia, chills, weight decrease, lacrimation increase, conjunctivitis, dry eye, blurred vision, dyspnea, epistaxis, cough, flatulence, abdominal distension, gastro-esophageal reflux, constipation, dry mouth, gastritis, increased hepatic enzymes, pruritus, dry skin, erythema, alopecia, night sweats, joint swelling.

Potentially serious: fluid retention, anasarca, edema (including brain, eye, pericard, abdomen, and lung), neutropenia, thrombocytopenia or anemia, pancytopenia, hemolytic anemia, hypokalemia, hyperkalemia, sepsis, cellulitis, fungal infection, upper respiratory tract infection, interstitial lung disease, pneumonia, pericardial/pleural effusion, pleuritic pain, pulmonary hypertension/hemorrhage/fibrosis, congestive heart failure, arrhythmia, atrial fibrillation, cardiac arrest, myocardial infarction, angina pectoris, pericarditis, cardiac tamponade, thrombosis/embolism, ileus/intestinal obstruction, pancreatitis, hepatic failure/necrosis, hepatitis, exfoliative dermatitis, angioneurotic edema, Stevens-Johnson syndrome, erythema multiforme, leukocytoclastic vasculitis, Sweet's syndrome, lichenoid keratosis, lichen planus, toxic epidermal necrolysis, anaphylactic shock, syncope, hypotension, hematoma, acute respiratory failure, acute renal failure, hemorrhage (including brain, eye, kidney, and gastrointestinal tract), melena, hematemesis, diverticulitis, colitis, inflammatory bowel disease, gastrointestinal perforation, ascites, gastric ulcer, tumor hemorrhage/necrosis, hip osteonecrosis/avascular necrosis, sciatica, optic neuritis, cataract, papilledema, glaucoma, hearing loss, Raynaud's phenomenon, increased intracranial pressure, peripheral neuropathy, depression, convulsions.

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