Longer treatment with cancer drug following removal of GI tumor results in improved survival

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Among patients with a high risk of recurrence of a gastrointestinal stromal tumor following surgery for its removal, patients who received imatinib (a drug to treat certain cancers) for 3 years instead of 1 had improved recurrence-free survival and overall survival, according to a study in the March 28 issue of *JAMA*.

"Gastrointestinal stromal tumors (GIST) are usually found in the stomach or the small intestine but can occur at any site along the gastrointestinal tract and rarely elsewhere within the abdominal cavity," according to background information in the article. "The malignancy potential of GIST varies from negligible in micro GIST to aggressive cancer." Treatment with imatinib for 12 months after surgery has improved recurrence-free survival (RFS), although recurrence of GIST is common during the first years following discontinuation of treatment, suggesting that 12 months of administration may be too short a time period.

Heikki Joensuu, M.D., of the Helsinki University Central Hospital, Helsinki, Finland, and colleagues examined whether adjuvant (following surgery) imatinib treatment for longer than 3 years might be beneficial compared to 1 year of administration for GIST patients who were considered to have a high risk of GIST recurrence. The randomized trial included patients with KIT (a gene)-positive GIST removed at surgery who were entered into the study between February 2004 and September

2008. Two hundred patients were assigned to the 12-month group and 200 to the 36-month group from 24 centers located in Finland, Germany, Norway, and Sweden. Patients were randomized to receive imatinib, 400 mg per day, orally for either 12 months or 36 months, started within 12 weeks of surgery.

The researchers found that recurrence-free survival was longer in the 36-month group compared with the 12-month group (5-year RFS, 65.6 percent vs. 47.9 percent). Fewer patients assigned to 36 months of imatinib administration died during the follow-up as compared with those assigned to the 12-month group (12 vs. 25, respectively), and overall survival was longer in the 36-month group (5-year survival, 92.0 percent vs. 81.7 percent, respectively).

The authors also found that a larger proportion of patients discontinued imatinib in the 36-month group for reasons other than GIST recurrence compared with the 12-month group (51 [25.8 percent] vs. 25 patients [12.6 percent], respectively; the reasons were adverse effect, patient preference, tumor histology not GIST, and other or unspecified reason). Almost all study patients had at least 1 adverse event recorded; most events were graded mild in severity.

The researchers add that the effect on overall survival was based on a relatively small number of deaths, and the study patients will continue to be followed up to confirm the overall survival benefit. "Because GIST recurrence is frequent after discontinuation of adjuvant imatinib, studies that evaluate still longer treatments are warranted, as are studies that address novel agents and their combinations."

Charles D. Blanke, M.D., F.R.C.P.C., of the University of British Columbia and British Columbia Cancer Agency, Vancouver, Canada, writes in an accompanying editorial that the U.S. Food & Drug Administration recently granted regular approval for adjuvant use of

imatinib in adults after resection of KIT-positive GISTs, and that the results of this trial has established 3 years of 400 mg of imatinib per day as the new standard of care for postoperative treatment of patients with resected high-risk GISTs.

"Some clinicians will use imatinib for a longer period, perhaps choosing to treat patients indefinitely. Investigators and clinicians alike will increasingly face the question of best postoperative duration of treatment with cytostatic, biologic targeted agents. However, correlative science provides little guidance. Laboratory biomarker studies may eventually provide information about which patients are unlikely to have recurrence , and thus are not capable of benefitting from any adjuvant therapy, but questions about curability or duration will not be answered by preclinical trials. As pathway-driven adjuvant therapy becomes more prolonged, increasing patients' tolerance of even low-grade toxicities will be critical to improve their adherence to expensive treatments that could last for decades."

More information: *JAMA*. 2012;307[12]:1265-1272.
JAMA. 2012;307[12]:1312-1314.