Editorial

Pediatric gastrointestinal stromal tumors: a commentary on the value of referral clinics for rare pediatric tumors

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Comment on: Weldon CB, Madenci AL, Boikos SA, *et al.* Surgical Management of Wild-Type Gastrointestinal Stromal Tumors: A Report From the National Institutes of Health Pediatric and Wildtype GIST Clinic. J Clin Oncol 2016:JCO2016686733. [Epub ahead of print].

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Gastrointestinal stromal tumors (GIST) are mesenchymal neoplasms of the gastrointestinal tract that originates from intestinal pacemaker cells, also known as interstitial cells of Cajal (1). Most cases are seen in adults between the 4th and 6th decade of life. Children and adolescents are rarely affected, and only 1.4% to 2.7% of all GISTs occur in this population (2). The most common clinical scenario in younger patients is the diagnosis of a gastric GIST that usually occurs in adolescent females (3). Pediatric GIST has unique clinical, biological and genetic features that are distinct from adulthood GIST (4). While most GISTs in adults have an activating mutation of the KIT or platelet-derived growth factor receptor (PDGFR) proto-oncogenes, this is only present in only 10% of pediatric GISTs. GISTs that lack KIT or PDGFR mutations are considered wild-type GISTs (WT-GISTs) (5). Several receptor tyrosine kinase inhibitors such as Imatinib have proven effective in treating GIST that shows KIT or PDGFR mutations (6). Treatment of GIST is based on surgical resection with negative margins, since it is resistant to chemotherapy and radiation. The addition of receptor tyrosine kinase inhibitors is recommended for patients with KIT or PDGFR mutations.

The rarity of this tumor and the lack of data supporting guidelines for the surgical management of WT-GIST encouraged the establishment of a WT-GIST clinic at the National Cancer Institute of the National Institutes of Health (NIH) in 2008. The NIH Clinical Center opened in 1953 and more than 500,000 clinical research participants have been involved since then. Patients come from all 50 states in United States and from around the world. Currently, there are about 1,600 clinical research studies in progress at the NIH Clinical Center. About half are studies of the natural history of disease, especially rare diseases such as WT-GIST.

In this issue of the *Journal of Clinical Oncology*, Weldon *et al.* (7) aimed to determine the optimal role of surgical intervention in the management in a large cohort of patients with WT-GIST. A total of 76 patients with a diagnosis of WT-GIST were included in this study. Clinical data were collected over a 7-year period. The WT-GIST clinic at NIH opened in 2008 and a multidisciplinary team evaluated these patients biannually. Inclusion criteria were having either a GIST diagnosis before 19 years of age or, for adults ages 19 years or older, known WT-GIST. Patients with KIT or PDGFR mutations were excluded from the study. Associations with event-free survival (EFS) were evaluated using the Kaplan-Meier method and Cox proportional hazards modeling. The female predominance in GIST was documented with only 24% of participants being males. Median age at diagnosis was 21 (range, 12–32) years. Most patients had gastric localized disease at diagnosis. Metastatic disease including liver, omentum, small bowel and other sites, was present at initial diagnosis in 26% of the participants. Locoregional (surrounding structures or

lymph nodes) disease was present in 12% of the patients at diagnosis. For patients with localized disease, complete surgical resection with negative margins (R0) was obtained in 93% of the cases. In contrast, R0 was only possible in 78% and 47% of patients with locoregional involvement and metastatic disease, respectively. Neoadjuvant chemotherapy and adjuvant tyrosine kinase inhibitors were used in 11% and 78% of patients, respectively.

Conclusions included that patients have prolonged survival, but EFS was 16.3%±5.5% at 10 years. Prognostic factors associated with decreased survival were tumor mitotic rate and presence of metastatic disease. In contrast, the status of microscopic resection margins and the type of gastric resection were not significantly associated with survival. In comparison with the adult GIST, WT-GIST shows a less aggressive behavior but it tends to recur locally, therefore it must be viewed within the spectrum of a chronic condition that requires long-term follow-up. Authors recommend minimizing the extent of resection in gastric GIST with wedge resection being the most appropriate surgical procedure. Patients were enrolled in a clinic protocol, in which clinical records were systematically obtained primary radiology and pathology data were independently reviewed by the NIH Pediatric and WT-GIST Clinic. This referral clinic model may represent a good method to help ensure prompt patient evaluation and treatment of this rare entity. Data obtained from this clinic may also help to guide future prospective clinical trials on rare tumors.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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