43.1. Gastrointestinal Stromal Tumor: Gastric and Omental

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Emerging Prognostic Factors for Clinical Care

Tumor Mutation

There may be differences in behavior among GISTs with different types of *KIT* and *PDGFRA* mutations. Because of limitations of the universal application of mutation studies (most importantly, their limited availability), mutations presently are not included in the AJCC staging system. Further research is needed to examine these and other prognostic factors in detail.

For GISTs at significant risk of recurrence, such as Stage III gastric GIST and Stage II-III small bowel GIST, 3 years of adjuvant imatinib is an international standard of care based on randomized clinical trial data, as of the publication of this staging system.[1] The decision regarding the use of adjuvant therapy is complicated by the mutation status of the primary tumor. For example, from existing data, *KIT* exon 9–mutant GISTs have a lower risk of recurrence than *KIT* exon 11–deleted GISTs, but the limited datasets available make inclusion of these data in the staging system premature.

KIT mutation status also may affect recommendations for therapy in the metastatic setting, for example, in comparing metastatic GIST with *KIT* exon 9 versus exon 11 mutation. Specific recommendations regarding dose and schedule of therapy are beyond the scope of the staging criteria. The prevalence of various *KIT* and *PDGFRA* mutations are depicted in Figure 43.1.[2]

GIST Nomogram

A nomogram has been developed based on tumor size, site, and mitotic rate to estimate the 2 and 5 year recurrence-free survival in GIST. The nomogram was derived from a retrospective cohort of 127 patients with localized, primary GIST who underwent surgical resection at Memorial Sloan-Kettering Cancer Center.[3] The nomogram was then validated in the original publication in a series of 148 patients at the Mayo Clinic and 212 patients in the Spanish National Sarcoma Registry. Subsequently, the nomogram was validated in three other publications.[4-6] The nomogram is available online at https://www.mskcc.org/nomograms/gastrointestinal. Note that surgery alone is curative in about 70% of patients with a GIST that is at least 3 cm in size (Figure 43.2). This method of risk assessment does not currently meet the AJCC quality criteria described in chapter 4, is currently not endorsed by AJCC, and will be re-evaluated in the future.

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Risk Assessment Models

The AJCC recently established guidelines that will be used to evaluate published statistical prediction models for the purpose of granting endorsement for clinical use.[7] Although this is a monumental step toward the goal of precision medicine, this work was published only very recently. Therefore, the existing models that have been published or may be in clinical use have not yet been evaluated for this cancer site by the Precision Medicine Core of the AJCC. In the future, the statistical prediction models for this cancer site will be evaluated, and those that meet all AJCC criteria will be endorsed.

Recommendations for Clinical Trial Stratification

It is recommended that primary GISTs be stratified by stage as well as tumor rupture. Metastatic GIST should be stratified by involvement of the liver only, peritoneum only, or both, as well as extra-abdominal metastasis. Consideration also should be given to mutation type, if possible, for primary and metastatic GISTs.

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