ISSN: 2157-2518
Journal of Carcinogenesis & Mutagenesis

OPEN ACCESS Freely available online

Commentary

Treatment Protocols for Intestinal Stromal Tumors

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DESCRIPTION

The protocols for treating GISTs, including those for limited-stage disease and chronic or metastatic disease.

Limited-stage disease with possible resection

The main course of treatment for GISTs that are localised or might be resectable is surgery. If high-risk endoscopic ultrasound signs are not present, patients with small GISTs (2 cm) may be managed with endoscopic surveillance. High-risk endoscopic ultrasound features include the following [1].

- A skewed border
- Cystic area
- Ulceration the echoegenic foci
- Heterogeneity

Neoadjuvant therapy: Neoadjuvant imatinib therapy is preferred for patients with comorbidities for surgery or tumours that are only partially resectable.

- Neoadjuvant therapy aims to shrink the tumour, which might make a complete surgical resection possible.
- The course of treatment should be continued until the maximum response, which usually takes between 10 and 12 months [2-4].
- Imatinib is typically administered 400 mg PO once daily. If tolerated, a dose of 800 mg PO daily can be recommended in patients with a known exon 9 KIT mutations.
- Platelet-derived growth factor receptor-alpha (PDGFRA) D842V mutation, succinate dehydrogenase (SDH) deficiency, or neurofibromatosis (NF)-associated GIST: Neoadjuvant imatinib will be less effective and is therefore not advised.
- Adjuvant therapy for high-risk patients: After complete gross resection of a CD117-positive GIST, Imatinib 400 mg PO daily for 3 years has demonstrated an improvement in overall survival and recurrence-free survival compared with a treatment period of one year.
- Adjuvant imatinib can continue to prevent (or delay) recurrences for up to five years, however nearly half of individuals who received treatment stopped taking it early due to side effects.
- It is not advised to use adjuvant imatinib in patients with PDGFRA D842V mutations, SDH deficiency, or NF-related GIST since it will be less effective.

Persistent or metastatic disease

Imatinib is the main therapy for metastatic GISTs. After a favourable response to preoperative imatinib, individuals with locally advanced or previously unresectable cancer, or those with modest disease progression on systemic therapy, may need surgery [5].

Recommended therapy

- Imatinib 400 mg PO once daily [17, 18, 19, 20]: The dose can be increased to 800 mg for individuals who have a known KIT exon 9 mutation. Disease progression while using 400 mg of imatinib PO daily: As tolerated, the dose may be increased to 800 mg (400 mg PO BID day).
- Sunitinib is a viable alternative for patients who have the known PDGFRA D842V mutation, which results in imatinib resistance. Dasatinib may also be active in this population, according to some data [6].
- Imatinib is not advised due to resistance in individuals with an SDH-deficient or NF-related GIST. Regorafenib or sunitinib would be potential treatments in this case.
- Sunitinib 50 mg PO daily for 4 weeks, followed by 2 weeks off (4/2 schedule); off-label continuous dosage at 37.5 mg PO daily has been shown to be more effective and to improve tolerance.
- Regorafenib is used for locally advanced, unresectable GISTs that are no longer responsive to imatinib or sunitinib. The recommended dosage is 160 mg PO daily for the first 21 days of each 28-day cycle.
- Avapritinib: 300 mg PO daily, continuing until disease progression or intolerable toxicity; recommended for unresectable or metastatic GIST carrying a mutation in exon 18 of the platelet-derived growth factor receptor alpha (PDGFRA), such as PDGFRA D842V.

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Received: 01-Sep-2022, Manuscript No. JCM-22-18338; **Editor assigned:** 05-Sep-2022, Pre QC No. JCM-22-18338; **Reviewed:** 19-Sep-2022, QC No. JCM-22-18338; **Revised:** 26-Sep-2022, Manuscript No. JCM-22-18338; **Published:** 03-Oct-2022, DOI: 10.35248/2157-2518.22.S34.004

Citation: Canelo H (2022) Treatment Protocols for Intestinal Stromal Tumors. J Carcinog Mutagen. S34:004.

- Ripretinib: recommended for patients with advanced GISTs who have previously had treatment with three or more kinase inhibitors, 150 mg PO daily until disease progression or intolerable effects.

Increasing ailment

Patients with progressing illness whose GISTs are resistant to imatinib, sunitinib, and regorafinib have little treatment options. The following are some potential strategies [7].

Enrollment in a clinical trial

- If all other treatments have failed, patients may be given a second chance with imatinib and sunitinib.
- For patients who do not benefit clinically from imatinib and sunitinib, use of sorafenib, dasatinib, or nilotinib.

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