Gastrointestinal stromal tumors (GIST): New treatment expectations

Dear Editor,

Gastrointestinal stromal tumors (GIST) have been known for over twenty years, but until ten years ago they were a heterogeneous group of neoplasms which included leiomyomas, leiomyosarcomas, leiomyoblastomas and schwannomas. They represent approximately 0.5-3% of all primary tumors of the gastrointestinal tract, only 5% of visceral sarcomas, but 80% of malignant tumors originated in the mesenchymal tract (1). The belief that these tumors are the “benign” form of the gastrointestinal neoplasms is widespread. However, the most commonly used classification -Fletcher, 2002 (2), based on the tumor size and the mitotic count by 50 high power fields- divided GIST in very low, low, medium and high risk of malignancy.

A review of the available literature showed that both medium and high risk-malignancy tumors are able to induce distant metastasis. Over the last ten years, eleven patients were diagnosed and operated in our hospital. Three of them died from metastatic disease: One of them presented a high risk GIST. Half of the four whose tumors were classified as medium-risk died due to the neoplasms. All remaining patients are currently asymptomatic and only one of them, with a medium risk-tumor originated in the small bowel, is still being treated with 400 mg of imatinib per day.

A new marker, which happens to be independent of KIT mutations and PDGFRα, has been recently discovered. It is a chloride channel protein denominated DOG1. It seems to have the same diagnostic sensitivity as other mutations that have been employed until now. DOG1 is especially useful in highly-suspected GIST with negative KIT staining (3,4). However, there was negativity for these two immunohistochemical markers (DOG1 and KIT) in 2.6% of the gastrointestinal tumors (3). In these cases, the protein kinase C theta (PKCtheta) could be used since it seems to be expressed in all GIST (5). Those two mutations (DOG1 and PKCtheta) are gaining importance for diagnosing GIST after a negative KIT, since an accurate diagnosis is crucial for a satisfactory treatment with imatinib.

The treatment of choice for primary disease is complete surgical resection (R0). The spread via the lymphatic system is not probable, therefore, it is not necessary to leave wide margins of resection or perform an extended lymphadenectomy. Sometimes it could be necessary to perform complex interventions (Mile’s abdominoperineal amputation, Whipple intervention) due to the tumor location (6,7). The fragmentation of the tumor may cause tumor implants, thus the most important aspect during the surgery is trying to avoid this situation (1). It would be equivalent to a R2 resection (6).

Instrumental manipulation could increase the risk of peritoneal dissemination. This is the reason why most authors accept

### Table I. Fletcher’s criteria of prognosis

<table>
<thead>
<tr>
<th>Size (cm)</th>
<th>Mitotic count (per 50 HPF*)</th>
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<tbody>
<tr>
<td>Very low risk</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Low risk</td>
<td>2-5</td>
</tr>
<tr>
<td>Medium risk</td>
<td>&lt; 5</td>
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<td></td>
<td>5-10</td>
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<tr>
<td>High risk</td>
<td>&gt; 5</td>
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<tr>
<td></td>
<td>&gt; 10</td>
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<tr>
<td>Any size</td>
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*HPF: High power fields.


9. Casali PG, Blay JY; ESMO/CONTICANET/EUROBONET Consen-


In GIST resistant to imatinib and sunitinib, the use of sorafenib, dasatinib, motesanib and nilotinib is being studied (13).

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References