Letter to the Editor

Pazopanib use preceding curative surgery in low rectal gastrointestinal stromal tumors after imatinib failure: A case report

DOI: 10.4103/sajc.sajc_183_18

Dear Editor,

Imatinib in neoadjuvant setting has shown improved outcomes in gastrointestinal stromal tumors (GISTs), especially when considered for longer duration.[1] Implementation of the same strategy to improvise resectability, sphincter preservations, and disease-free survival outcomes in rectal GIST was published from our center.[2] Sunitinib in the second line and regorafenib in the third line are the approved agent for the treatment of imatinib-resistant or intolerant advanced GIST and imatinib followed by sunitinib failure/intolerant advanced GIST, respectively.[3,4] Pazopanib was shown to have efficacy in sunitinib intolerant or failure patients after imatinib use.[5-7] Toxicities and cost of sunitinib/regorafenib may hinder the use of these agents, especially in resource-limited settings of India.

Surgical resection of GIST after failure of imatinib but clinical benefit with the use of sunitinib has been explored.[8,9] However, there are no prospective studies in neoadjuvant setting on the use of agents other than imatinib when it has failed or it is intolerable. We report an imatinib nonresponsive case of locally advanced rectal GIST who could undergo sphincter-preserving R0 resection after the use of pazopanib. A patient could not afford sunitinib or regorafenib and was not willing for exenterative surgery.

A 25-year-old man suffered from bleeding per rectum for 1 year before presenting to our institute. Per rectal digital examination revealed a growth 2 cm above the anal verge. Colonoscopy revealed an irregular tumor starting from anal verge and extending for 12 cm, scope could be negotiated beyond the tumor, and rest of colonic mucosa was normal. Contrast-enhanced computed tomography (CT) showed a large irregular rectal mass obliterating the rectal lumen infiltrating into adjacent fat planes with no enlarged lymph nodes. Rectal mass biopsy showed it to be rectal GIST with epithelioid morphology, and on immunohistochemistry, the tumor cells were diffusely positive for C-KIT and DOG-1 whereas negative for S100 and SMA. Magnetic resonance imaging (MRI) showed exophytic large lesion in the lower rectum, anterior left lateral wall, MR fat, and fascia involved with right levator involvement. Kit and PDGFRA mutation by sequencing test were of wild type.

Based on these findings, the patient was started on neoadjuvant imatinib at 400 mg/day. He tolerated the therapy well with only Common Terminology Criteria for Adverse Events of the National Cancer Institute, version 4.03 (CTCAE-NCI) Grade 1[10] nausea and Grade 2 anemia. Response assessment MRI [Figure 1] at the end of 3 months of therapy showed significant interval increase in the size and extent of the endoluminal component, while the exoluminal nodular component shows a mild increase in size. The large nodular-proliferative endoluminal component was distending and obstructing the lumina. The mass infiltrated MRF with anterior displacement prostate, seminal vesicle, and base of the bladder with effacement of the intervening fat planes without signs of infiltration.

The disease started fungating over anal area leading to pain and debilitation. Due to poor nutritional status and clinical disease progression, the patient's general condition deteriorated. The dose of IM was increased to 800 mg/day, which the patient could not tolerate. As the patient had nonmetastatic disease with local progression, exenterative surgery was offered for which he was not willing. Hence, he was offered next line of therapy with palliative intent after the detailed discussion about the pros and cons and the options available. Sunitinib or regorafenib was considered, but the patient could not afford the same. Pazopanib at 600 mg/day was started, and the patient benefitted clinically and radiologically with the treatment. The patient had CTCAE version 4.03[10] Grade 3 hand-foot syndrome, Grade 2 mucositis, Grade 3 skin pigmentation, and Grade 1 alopecia and graying of hairs. Clinically, fungating mass disappeared and rectal pain decreased significantly.

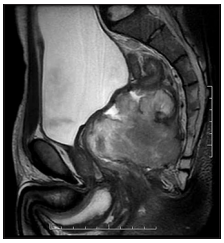

Figure 1: Prepazopanib magnetic resonance imaging suggestive of bulky disease

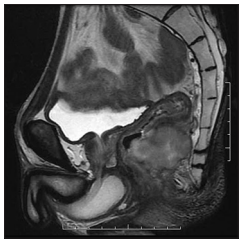

Figure 2: Postpazopanib magnetic resonance imaging suggestive of significant response

Post 3 months of pazopanib treatment, MRI [Figure 2] suggested lobulated mass, 3.0 cm away from the anal verge, and as compared to the previous scan, there was a significant decrease in the size of the mass. The patient underwent laparoscopic intersphincteric resection (lap ISR). Post-ISR, the patient could not tolerate adjuvant imatinib. In view of progression of the disease on imatinib and no supportive evidence for adjuvant pazopanib available, the patient was observed. Post 19 months of surgery, positron emission tomography–contrast-enhanced CT did not show any evidence of recurrence. Stoma closure surgery was performed, and apart from some minor complaints, the patient is doing well.

Pazopanib has a better quality of life profile and safety as shown in metastatic renal cell carcinoma (mRCC).[11] Pazopanib is available in India at 20% of the cost of sunitinib. The cost-effectiveness analysis of pazopanib versus sunitinib in mRCC patients showed superiority of pazopanib in most of the domains.[12] This case report describes the only report of the use of pazopanib in locally advanced low rectal GIST preceding curative R0 resection along with anorectal sphincter preservation, which did not appear feasible after imatinib failure.

Curative surgery may be a feasible option after pazopanib use in imatinib nonresponsive GIST patient when sunitinib or regorafenib is economically not feasible.

Consent

A well-informed written consent was obtained.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Nikhil Pande, Omshree Shetty[1], Mounika Boppana, Anant Ramaswamy, Avanish Saklani[2], Nitin Shetty[3], Vikas Ostwal

Departments of Medical Oncology, [1]Pathology, [2]Surgical Oncology and [3]Interventional Radiology, TMH, Mumbai, Maharashtra, India

Correspondence to: Dr. Vikas Ostwal,
E-mail: dr.vikas.ostwal@gmail.com

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How to cite this article: Pande N, Shetty O, Boppana M, Ramaswamy A, Saklani A, Shetty N, *et al*. Pazopanib use preceding curative surgery in low rectal gastrointestinal stromal tumors after imatinib failure: A case report. South Asian J Cancer 2019;8:51.