Strategies for Equality in Cancer Care in Low- and Middle-Income Countries
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Gastrointestinal stromal tumor (GIST) represents the most frequently occurring malignant neoplasia originating from mesenchymal cells, with an incidence of 12 cases per million people per year.1 Oncogenic gain-of-function sequence variants in the tyrosine kinases KIT or PDGFRA drive most GIST cases (80%-85%).2 Therapy for patients with GIST has been revolutionized by the development of small-molecule inhibitors targeting these kinases. Imatinib mesylate is currently the drug of choice for adjuvant therapy in patients at high risk of relapse, neoadjuvant treatment for those with high tumor burden, and first-line palliative systemic therapy for metastatic GIST.2 For patients with disease refractory to imatinib, other kinase inhibitors have demonstrated a benefit in randomized phase 3 trials, including sunitinib malate.2 The pivotal trials leading to approval of imatinib and sunitinib, both in the adjuvant and metastatic settings, were conducted in the US and Europe, with no patients enrolled in low- and middle-income countries (LMICs).3

Wagner et al4 describe the demographic characteristics, treatment duration, and survival of patients with a histologically confirmed diagnosis of GIST with immunohistochemistry positivity for KIT who received imatinib and sunitinib through 2 expanded-access programs. A total of 12,015 patients from 66 countries received imatinib, mostly (9866 [82.1%]) for unresectable or metastatic disease. Patients were younger when compared with those from high-income countries. The findings of this study suggest that oral targeted therapy for patients with GIST in LMICs may be feasible and safe, and the outcomes are similar to those reported in Europe and North America. Specifically, the median overall survival for patients treated with imatinib for unresectable or metastatic disease was 5.8 (95% CI, 5.6-6.1) years, and the median overall survival for those receiving sunitinib for metastatic or unresectable patients was 2.0 (95% CI, 1.5-2.5) years. There are several limitations to the analysis, which reports nonrandomized, unblinded clinical data from a program with the primary goal of providing access to medications, not collecting prospective efficacy and safety data.

The efficacy of imatinib in phase 3 randomized trials and clinical data, including LMICs, highlights the importance of securing continuous access to this medication for patients diagnosed with GIST worldwide. In addition, the results by Wagner et al4 can serve as an example to fuel the delivery of additional highly efficient targeted therapies across the globe. A recent international survey5 evaluated the access to essential cancer medications, of which 20% were targeted drugs. A total of 948 oncologists from 82 countries completed the survey, focusing on the availability and financial risk associated with cancer medications in LMICs.5 The results highlighted that in low- and lower middle-income countries, the availability of the top 20 high-priority cancer medications ranged from 9% to 54%, and there was a significant risk of catastrophic expenditure, with 13% to 68% of respondents indicating a substantial financial burden associated with these medications.5 Expanded-access programs are key for immediate access to treatment, but the next step is establishing a long-term support structure that can adapt to the evolving health care needs of patients with GIST. In the above-cited survey, only 36% of respondents from LMICs listed imatinib as universally available, and 50% identified that patients requiring this medication face significant out-of-pocket expenses.5

One additional important aspect of ensuring access to targeted therapies is the availability of biomarkers to identify patients most likely to benefit, making sure resources are allocated efficiently. Specifically for patients with GIST, diagnostic testing for KIT and PDGFRA sequence variants ensures appropriate patient selection, optimizing outcomes and minimizing unnecessary exposure to potentially ineffective therapies for tumors harboring resistant phenotypes, such as wild-type GIST.

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and PDGFRA exon 18 D842V sequence variant. Testing has been shown to be cost-effective in different settings, including LMICs. A recent elegant analysis demonstrated that molecular tests to guide initiation of adjuvant imatinib therapy in patients diagnosed with high-risk GIST reduced costs, considering the cost of preventing an event of available next-generation sequencing strategies in both the public and private health care systems in Brazil.

In conclusion, the findings presented by Wagner et al illustrate a clear pathway to improving outcomes for patients with GIST worldwide through the provision of targeted therapies. However, the journey does not end with temporary access. The continuous availability of tyrosine kinase inhibitors, coupled with the essential integration of KIT and PDGFRA sequence variant testing, represents the next frontier in the global treatment of GIST.

ARTICLE INFORMATION
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REFERENCES