The Cost Impact of Increased Molecular Testing Rates for the Treatment of Patients with Gastrointestinal Stromal Tumors

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Background

- Gastrointestinal stromal tumors (GIST) are a rare type of sarcoma, driven by activating genetic mutations encoding tyrosine kinase receptors for c-Kit (CD117, *KIT*; 75%–80% of diagnoses) or platelet derived growth factor receptor alpha (*PDGFRA*; 5%–10%)[1,2]
- The total number of US GIST cases each year is estimated at 2,300, with *PDGFRA* exon 18 mutations representing the majority of *PDGFRA* mutations overall[3,4] and *KIT* exon 9 mutations driving around 6.9-7.5% of all GIST cases[3,5]
- Testing for *PDGFRA* mutational status is strongly recommended in US clinical guidelines[6]
  - Observed lack of response for the majority of patients with *PDGFRA* exon 18 mutations, including D842V, among patients who take imatinib in the 1L metastatic setting[2]
  - Improved survival has been demonstrated for *KIT* exon 9 patients when treatment dosing is increased[7]
- Estimation of testing costs is relevant for healthcare decision makers and is expected to be low
  - In a Belgian study, GIST testing cost burden was low, in adjuvant and advanced disease.[8] Our study uses a US context and includes adverse event (AE) cost

Objective

- Estimate the cost impact associated with an increase in molecular testing rates of *PDGFRA* exon 18 and *KIT* exon 9 for US GIST patients, including the effects of treatment allocation decisions and AEs

Methods

Study design

- A model was developed in Microsoft Excel® to estimate the cost impact associated with molecular testing in GIST patients for *PDGFRA* exon 18 and *KIT* exon 9 mutations, on a hypothetical US health plan with 1 million covered lives, on a 12-month incidence basis. All costs are presented in 2019 USD ($).
- The model compared costs based on observed current testing rates at diagnosis to a scenario where 100% of patients are tested. Testing results determine treatment allocation and resulting monthly pharmacy and AE costs (**Tables 1** and **2**)

Patient population

- Patients with metastatic / non-resectable GIST, as well as adjuvant GIST, with *PDGFRA* exon 18 or *KIT* exon 9 mutations, were selected for inclusion, on the basis that the prescribed treatment regimen would vary based on the test results
- Patient flow based on testing results is illustrated in **Figure 1**

Table 1: Overview of the GIST cost of testing model

Parameter	Description
Audience	• Health plans, in particular population-based decision makers
Perspective	• US health plan (commercial, Medicare, Medicaid, or a mix)
Epidemiology	• Incidence-based
Time horizon	• One year
Population	• Patients with GIST, adjuvant or metastatic / non-resectable disease
Key inputs	• Incidence of GIST • *PDGFRA* exon 18 and *KIT* exon 9 mutation and testing rates (diagnosis and by line) • Costs: mutational testing[9,10] imatinib drug,[11] AEs[12] • Duration of treatment

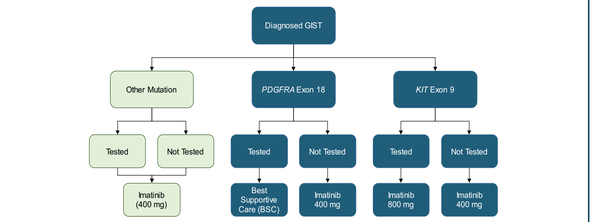
Abbreviations: AE, adverse event; GIST, gastrointestinal stromal tumor; KIT, v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog; PDGFRA, platelet derived growth factor receptor alpha.

Table 2: Key model assumptions

Assumption	Description
Patient population	• Base case population of 69% Commercial, 22% Medicare, and 9% Medicaid • Newly diagnosed patients with adjuvant, metastatic or non-resectable GIST
GIST incidence	• 11 per million members
Mutational test used	• PCR-based single gene test ($330 per gene)
Mutational testing rates	• *PDGFRA* exon 18: 49% tested at diagnosis, or after progression to either 2L or 3L (63% and 73%, respectively) • *KIT* exon 9: 60% tested, at diagnosis • Patients are tested a maximum of once for each mutation
Treatment duration	• Adjuvant: 36 months • Advanced/metastatic: mPFS from clinical trials (*PDGFRA* exon 18: same duration as imatinib-treated patients for patients tested, 6.4 months[2] for patients not tested; *KIT* exon 9: 19.1 months[7] for patients tested, 6.1 months[7] for patients not tested)
PDGFRA exon 18 + treatment	• Optimal treatment allocation assumed to be BSC, given the lack of response , with imatinib in *PDGFRA* Exon 18 D842V, and potential for adverse events[8]
KIT exon 9 + treatment	• Optimal treatment allocation assumed to be imatinib 800 mg[8]

Abbreviations: BSC, best supportive care; GIST, gastrointestinal stromal tumor; KIT, v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog; mPFS, median progression-free survival; PCR, polymerase chain reaction; PDGFRA, platelet derived growth factor receptor alpha.

Figure 1: Flow of GIST patients through *PDGFRA* exon 18 and *KIT* exon 9 testing



*The same patient flow is used for adjuvant and metastatic / non-resectable GIST.

Abbreviations: AE, adverse event; GIST, gastrointestinal stromal tumor; KIT, v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog; PDGFRA, platelet derived growth factor receptor alpha.

Results

Base case analysis cost impact

- An increase in testing rates to 100% for both mutation types is associated with a potential annual cost increase of $15,213 per million members, or $0.015 per member per year (PMPY)
- Increased costs in the base case are driven by increased dosing for exon 9 patients, and longer progression-free survival (PFS)
- Inclusion of only *PDGFRA* exon 18 testing results in a cost saving of $0.008 PMPY due to lower pharmacy costs
- For *PDGFRA* exon 18 and *KIT* exon 9 molecular testing combined, 10 additional patients need to be tested for one patient to receive optimized treatment
- The magnitude of the cost impact associated with increased testing remains small across all plan types

Table 3: Cost impact of increasing *PDGFRA* exon 18 and *KIT* exon 9 molecular testing – base case analysis

Potential cost impact and clinical value

Net potential cost impact
$0.015 PMPY

Number needed to test for one patient to receive optimized treatment
10 patients

Scenario	Pharmacy costs	Testing costs	AE costs	Total cost impact	Number of optimized patients
Current testing rate	$64,899	$4,517	$3,969	$73,385	0.61
Increased testing rate	$77,656	$7,265	$3,677	$88,598	1.08
Impact of higher testing rate	$12,758	$2,748	-$293	$15,213	0.47

Abbreviations: AE, adverse event; GIST, gastrointestinal stromal tumor; KIT, v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog; PDGFRA, platelet derived growth factor receptor alpha; PMPY, per member per year.

Table 4: Cost impact of increasing *PDGFRA* exon 18 molecular testing only

Potential cost impact and clinical value

Net potential cost impact
$-0.008 PMPY

Number needed to test for one patient to receive optimized treatment
31 patients

Scenario	Pharmacy costs	Testing costs	AE costs	Total cost impact	Number of optimized patients
Current testing rate	$8,614	$2,338	$830	$11,782	0.16
Increased testing rate	$0	$3,632	$0	$3,632	0.33
Impact of higher testing rate	-$8,614	$1,295	-$830	-$8,150	0.17

Abbreviations: AE, adverse event; GIST, gastrointestinal stromal tumor; PDGFRA, platelet derived growth factor receptor alpha; PMPY, per member per year.

Limitations

- Ayvakit™ (avapritinib) has recently been approved, which is now likely to represent the optimal treatment allocation for *PDGFRA* exon 18 positive patients. A scenario analysis was conducted, which showed a resulting cost impact of increased testing of $0.08 PMPY, due to higher pharmacy cost and significantly longer duration of drug treatment and PFS
- Molecular testing is assumed to have 100% diagnostic accuracy, with no false positives or false negatives

Conclusions

- Increased molecular testing in GIST is associated with minimal additional cost and a meaningful increase in the number of patients receiving optimized treatment
  - Estimated to be under $0.02 PMPY, even if KIT exon 9 testing is included in addition to *PDGFRA* exon 18
  - Increasing *PDGFRA* exon 18 testing alone may even lead to modest cost savings
- The major driver of estimated cost impact is pharmacy costs, but only a minority is directly due to an increased testing costs
- Improved treatment can be achieved with a moderate amount of additional test utilization, estimated at 10 additional patients tested for one patient to receive optimized treatment
- Results suggest that the economic impact associated with *PDGFRA* exon 18 and *KIT* exon 9 testing should not be barrier to an increase in testing rates in this indication

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Disclosures

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QR Code

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