Budget Impact Analysis of AYVAKIT™ (avapritinib) in Patients with Gastrointestinal Stromal Tumors and a *PDGFRA* Exon 18 Mutation

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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*; ~70% of diagnoses) or platelet derived growth factor receptor alpha (*PDGFRA*; 10%)[1,2] The most common PDGFRA mutation is the PDGFRA D842V mutation on exon 18
- Estimates vary, but the total number of new US GIST cases per year is considered to be a few thousand[3,4]
- AYVAKIT (avapritinib) is a precision therapy designed to be a selective and potent inhibitor of KIT and PDGFRA mutant kinases. In January 2020, avapritinib received FDA approval for the treatment of unresectable or metastatic PDGFRA exon 18 GIST
- NCCN guidelines recommend avapritinib for unresectable/metastatic GIST with *PDGFRA* exon 18 mutations and for patients progressing after treatment with imatinib, sunitinib, and regorafenib given the following:[5]
  - Observed lack of response for the majority of patients with *PDGFRA* D842V mutations, among patients who take imatinib in the 1L metastatic setting;[2] and
  - Reported suboptimal tolerability of other available treatment options for patients with *PDGFRA* D842V mutations (83% and 99% reporting treatment-related AEs following 2L and 3L therapy with sunitinib and regorafenib respectively)[6,7]
- Evaluation of the economic impact of a new therapy for unresectable or metastatic GIST is relevant for patients, payers, and healthcare decision-makers

Objective

- Quantify the incremental budget impact of the introduction of avapritinib for the treatment of adults with unresectable or metastatic GIST harboring a *PDGFRA* exon 18 mutation in a US healthcare plan

Methods

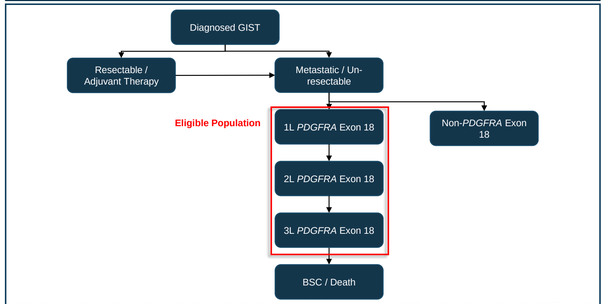
Study design

- A model was developed in Microsoft Excel® to estimate the budget impact of avapritinib for the treatment of adult patients with unresectable or metastatic GIST with a *PDGFRA* exon 18 mutation, for a hypothetical US health plan with 1 million covered lives, over a 3-year time horizon. All costs are presented in 2019 USD ($)
- The model included costs for testing, drug acquisition, monitoring, adverse events, as well as post-progression pharmaceutical treatment in up to 2 subsequent lines for those with a *PDGFRA* exon 18 mutation. The estimated budget impact was calculated based on the difference between the total costs of scenarios with and without avapritinib

Patient population

- Patients with metastatic/unresectable GIST with a *PDGFRA* exon 18 mutation, including D842V mutations, were included in the analysis
- Patient flow is illustrated in **Figure 1** and health plan mix is shown in **Table 2**

Figure 1: Eligible GIST population



Abbreviations: 1L, first-line of therapy; 2L, second-of therapy; 3L, third-line of therapy; BSC, best supportive care; GIST, gastrointestinal stromal tumors; *PDGFRA*, platelet-derived growth factor receptor alpha.

Table 1: Overview of the GIST avapritinib Budget Impact Model (BIM), *PDGFRA* Exon 18

Parameter	Description
Perspective	• US health plan (commercial, Medicare, Medicaid, or a mix)
Time horizon	• Three years
Population	• GIST patients, with metastatic or unresectable disease, who have a *PDGFRA* exon 18 mutation
Treatment options	• Avapritinib, imatinib, sunitinib, regorafenib, nilotinib
Key inputs	• GIST incidence[8] • *PDGFRA* exon 18 mutation rate[9] • Disease progression, by line[10-11] • Molecular testing rate • Duration of treatment with each drug[2] • Market share of each drug[11] • Economic inputs (drug, testing/monitoring, AE)[11-15]

Abbreviations: GIST, gastrointestinal stromal tumor; *PDGFRA*, platelet derived growth factor receptor alpha; AE, adverse event.

Table 2: Key model assumptions

Assumption	Description
Patient population	• US 1 million member plan with a base case population mix of 69% commercial, 22% Medicare, and 9% Medicaid • A constant population growth rate of 0.6% per year assumed
Costs	• All cost inputs are in nominal 2019 US dollars, including drug acquisition costs • No discounting of future costs or adjustments made for anticipated future inflation
Disease progression	• Model takes into account patients who decline drug therapy or die before each successive line of treatment
Mutational testing	• The model assumes that the introduction of avapritinib will increase *PDGFRA* exon 18 testing rates (user-modifiable; base case = 20% increase over 3 years)
Treatment duration	• Treatment duration for each drug regimen is assumed to be equal to mPFS • Where mPFS is not available in exon 18, data used comes from GIST patients with a *PDGFRA* exon 18 D842V mutation
Post-progression costs	• Post-progression costs are weighted based on the proportion of time spent in post-progression at each line and the market share of each comparator

Abbreviations: *PDGFRA*, platelet derived growth factor receptor alpha; mPFS, median progression-free survival; GIST, gastrointestinal stromal tumor.

Results

Base case analysis outcomes

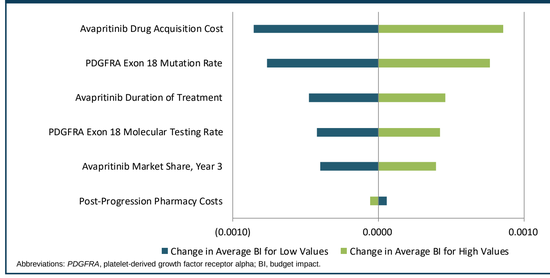
- In the hypothetical base case 1 million member plan, 0.07 new GIST *PDGFRA* exon 18 patients per year were estimated to be eligible for treatment
- With avapritinib available, the average total incremental annual plan costs in Years 1, 2, and 3 were $10,984, $27,972, and $46,961, respectively (per-member per-month $0.001, $0.002, and $0.004, respectively)
- Adopting avapritinib decreased post progression costs by $577 in Year 1, $2,103 in Year 2, and $3,711 in Year 3
- The increased rates of molecular testing assumed in the model resulted in an incremental health plan testing cost of $453 in Year 3 of avapritinib availability
- Sensitivity analyses revealed that the model is most sensitive to the cost of avapritinib followed closely by the *PDGFRA* exon 18 mutation rate (**Figure 2**)

Table 3: Budget Impact of Avapritinib Adoption in a 1 Million Member Combined Commercial, Medicare, and Medicaid Plan

Budget Impact ($)[a,b]	Year 1	Year 2	Year 3
Total Cost with Avapritinib Available	$19,271	$41,245	$65,250
Of Which are Post-Progression Costs	$1,726	$5,150	$8,522
Total Cost without Avapritinib Available	$8,287	$13,273	$18,289
Of Which are Post-Progression Costs	$2,304	$7,253	$12,233
Incremental Budget Impact, Total	$10,984	$27,973	$46,961
Change in Post-Progression Costs	-$577	-$2,103	-$3,711
Incremental Budget Impact (PMPM)	**$0.001**	**$0.002**	**$0.004**

[a]The budget impact calculation is presented in 2019 USD and does not adjust for inflation in subsequent years
[b]No discounting factor is used in the budget impact calculation
Abbreviations: PMPM, per member per month

Figure 2: Sensitivity Analysis, Year 3 (Change in Budget Impact, PMPM)



Abbreviations: *PDGFRA*, platelet-derived growth factor receptor alpha; BI, budget impact.

Limitations

- Duration of treatment for avapritinib and comparator therapies was based on limited data in *PDGFRA* exon 18. For some treatments, data was based on studies in any *PDGFRA* mutation, or in *PDGFRA* D842V
- Testing costs were assumed to be single-gene PCR tests and do not include next-generation sequencing (NGS) tests, which may potentially increase testing costs
- Healthcare resource utilization costs for pre- and post-progression states were not included as data for metastatic GIST were not found. If included, these are likely to reduce the budget impact, since avapritinib patients on average spend less time in the post-progression state, which is typically more costly

Conclusions

- The number of patients eligible for avapritinib is small with an annual incidence of 0.07 patients with GIST with *PDGFRA* exon 18 mutations per 1 million members in a typical plan
- Adopting avapritinib would have a minimal budget impact, with an incremental PMPM of $0.004 in Year 3
- The cost increase associated with avapritinib is mainly driven by the longer mPFS for avapritinib of 29.5 months vs. comparator mPFS of 6.4 months
- The cost increase associated with avapritinib is partially offset by reduced post-progression costs (avoided or delayed) with avapritinib available
- The increased cost of molecular testing calculated in the model is minimal at $453 in Year 3
- Key model sensitivities include: drug price, treatment duration, and market share

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Disclosures

This research was funded by Blueprint Medicines Corporation. Blueprint Medicines reviewed and provided feedback on the poster. The authors had full editorial control of the poster and provided their final approval of all content. RM, CN and ES are employees of and hold equity interest in Blueprint Medicines. DP, AM, DN and AG are employees of Analysis Group, a consulting firm retained by Blueprint Medicines

Acknowledgements

The authors would like to acknowledge Sedge Lucas, an employee of Analysis Group, for developing the poster

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Presented at the Virtual International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conference, May 18-20, 2020