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Integrated Budget Impact Analysis of Introducing Selpercatinib as a Tumor-Agnostic Treatment Option for Patients with *RET*-Altered Solid Tumors in the United States

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Background

- Oncogenic alterations in REarranged during Transfection (*RET*) gene are reported in multiple solid tumor types.[1-5]
- Selpercatinib, a highly selective and potent *RET* kinase inhibitor, was initially approved by the US FDA for *RET* fusion-positive non-small cell lung cancer (NSCLC), thyroid cancer (TC), *RET*-mutant medullary TC (MTC).[6,7]
  - Subsequently approved for other *RET*-fusion positive tumors.[7-9]
- Budget impact analyses provide comprehensive economic assessment in terms of affordability of new healthcare interventions and are increasingly used by payers for making formulary decisions.[10-12]
- However, no literature is available describing approaches to develop tumor-agnostic BIMs for a single treatment (Tx).[13]

Model Overview

Table 1: Model Inputs – Base Case

Model Characteristic	Description
Time Horizon	3 years
Patient population	• 19 *RET*-altered tumor types* (included based on literature that reported potential *RET*-alterations across tumor types, and restricted to solid tumors).[14] • Eligible patient population for all tumor types were determined individually prior to integrating results. • Derived from the US epidemiological statistics by applying methodology as previously published.[13,15]
Perspective	Payer (Commercial and Medicare)
Plan members	1,000,000
Patients tested, %	100% testing for *RET* (assumed to avoid under-estimation)
Comparator costing approaches	**a) Micro-costing for proxy comparator (base case):** a tumor-specific Tx or regimen selected to be a representative comparator for each disease; • Pralsetinib (another *RET* inhibitor) was included as comparator per its FDA-approved indications. **b) Published literature-based comparator costs:** average Tx costs across diseases, wherever available.
Market share assumptions	• Selpercatinib: 65%, 70%, and 75% in years 1, 2, and 3 (from proxy Tx). • Wherever included, pralsetinib market share was constant across three years (25%).
Costs	Inflated to 2022 USD

**NSCLC, pancreatic cancer, colorectal cancer, MTC, TC, salivary gland cancer, cholangiocarcinoma, gastric cancer, small intestine cancer, ovarian cancer, breast cancer, prostate cancer, xanthogranuloma, melanoma skin cancer, non-melanoma skin cancer, sarcoma, pulmonary carcinosarcoma, carcinoid, carcinoma of unknown primary.*
Costs are reported for individual years and thus are not discounted. Guidelines for the development of budget impact models recommend against discounting.[19]
The iBIM was customizable to conduct user-preferred analyses integrated across all or scenario-specific selected tumors.

- **Other model characteristics:** cost of drugs and administration,[16,17] dosing regimens,[18-20] Tx related costs (monitoring, supportive care, and administration costs), and adverse event (AE) related costs.
- **One-way sensitivity analysis (OWSA):** performed for both Commercial and Medicare perspectives (at year 1, 2, and 3) to assess uncertainty associated with model parameters and key assumptions.
- **Scenario Analyses:**
  - ***Scenario 1:*** Assumed *RET* testing rate at 50%.
  - ***Scenario 2:*** Gastrointestinal tumor specific scenario (GI-specific; included pancreatic cancer, colorectal cancer, cholangiocarcinoma, gastric cancer, and small intestine cancer).

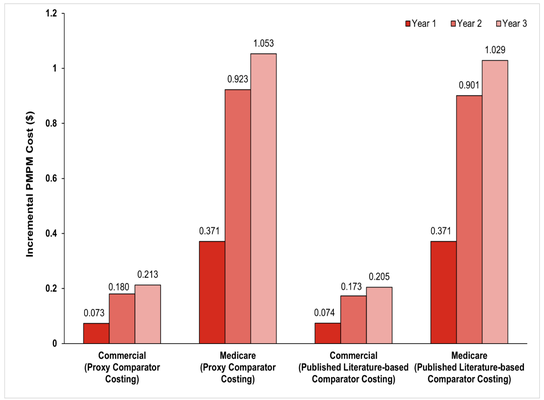
To develop an integrated BIM (iBIM) in the US to estimate:
the number of patients eligible for Tx with selpercatinib; and
the potential impact on US third-party payers' formulary budgets of introducing selpercatinib for RET-altered solid tumor Tx.

Table 2 (Base Case): Number of Patients with Positive RET-Altered Tumor (per million)

Tumor	Estimated Number of Patients with Positive *RET*-Altered Tumors Eligible for Tx	
	Commercial	Medicare
NSCLC (1L and 2L+)	5.84	34.37
MTC (1L and 2L+)	1.16	2.73
TC (1L and 2L+)	1.34	3.51
Pancreatic	0.27	1.5
Colorectal	1.58	6.57
Salivary	0.09	0.38
Cholangiocarcinoma	0.01	0.03
Gastric	0.05	0.22
Small Intestine	0.04	0.17
Ovarian	0.32	1.32
Breast	0.06	0.20
Prostate	0.14	0.66
Xanthogranuloma	0.01	0.01
Melanoma Skin	0.01	0.03
Non-melanoma Skin	0.02	0.26
Sarcoma	0.03	0.08
Pulmonary Carcinosarcoma	0.37	2.10
Carcinoid	0.27	1.2
Unknown Primary	0.09	0.48
Total	**11.68**	**55.82**

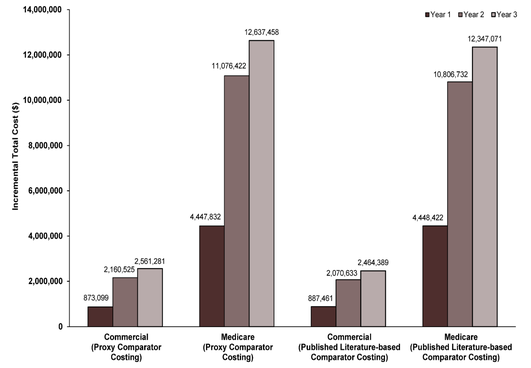
Patients included are per 1-million-members.1L: first-line; 2L+: second-line and beyond: NSCLC: non-small cell lung cancer; MTC: medullary thyroid cancer; RET: REarranged during Transfection; TC: thyroid cancer.

Figure 1: Incremental PMPM Cost (All Tumor Types)



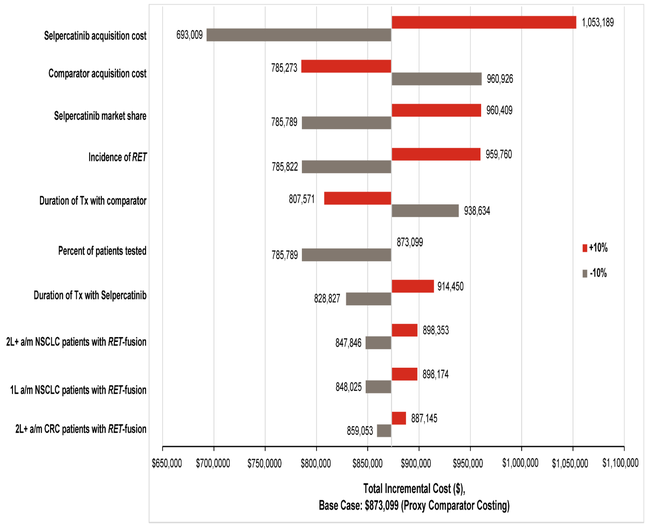
PMPM: Per Member Per Month. Incremental Cost: cost with selpercatinib – cost without selpercatinib

Figure 2: Incremental Total Cost (All Tumor Types)



Incremental Cost: cost with selpercatinib – cost without selpercatinib

Figure 3: OWSA (Base-case ± 10%) – Commercial (Year 1)



1L: first-line; 2L+: second-line and beyond; a/m: advanced/metastatic; BC: breast cancer; CCA; cholangiocarcinoma; MTC: medullary thyroid cancer; OWSA: one-way sensitivity analyses; RET: REarranged during Transfection. Range: -10% to +10% from base-case.

Table 3: Scenario Analyses

Scenario	Number of patients, (per million) Commercial		Number of patients (per million), Medicare		Incremental Cost ($)	Costing Method	Commercial			Medicare		
	Eligible for Tx	Selp. Treated	Eligible for Tx	Selp. Treated			Y1	Y2	Y3	Y1	Y2	Y3
50% *RET* Testing	5.84	3.79 (Y1); 4.09 (Y2); 4.38 (Y3)	27.91	18.14 (Y1); 19.54 (Y2); 20.93 (Y3)	PMPM	Proxy	0.036	0.09	0.107	0.185	0.462	0.527
						Published Literature	0.037	0.086	0.103	0.185	0.45	0.514
					Total Cost	Proxy	436,550	1,080,262	1,280,640	2,223,916	5,538,211	6,318,729
						Published Literature	443,731	1,035,316	1,232,195	2,224,211	5,403,366	6,173,536
GI-tumor Specific	1.94	1.26 (Y1); 1.36 (Y2); 1.46 (Y3)	8.49	5.52 (Y1); 5.94 (Y2); 6.37 (Y3)	PMPM	Proxy	0.013	0.014	0.015	0.062	0.067	0.072
						Published Literature	0.017	0.018	0.02	0.073	0.078	0.084
					Total Cost	Proxy	156,492	168,530	180,568	748,268	805,827	863,386
						Published Literature	205,969	221,813	237,656	873,260	940,434	1,007,608

PMPM: Per Member Per Month; Proxy: Proxy Comparator Costing; Published Literature: Published Literature-based Comparator Costing; RET: REarranged during Transfection; Selp.: Selpercatinib; Y: Year. All values are presented in terms of 2022$. Incremental Cost: cost with selpercatinib – cost without selpercatinib.
GI-tumors included: pancreatic cancer, colorectal cancer, cholangiocarcinoma, gastric cancer, and small intestine cancer.

Summary of Results and Conclusions

- This iBIM for selpercatinib included 19 solid tumor types and the conceptual approach implemented in this study serves as a proof of concept for developing BIMs for tumor-agnostic (multi-tumor) indications in the future.
- Number of patients with *RET*-altered solid tumors eligible for Tx in third-party US payer plans was low **(Table 2)**.
  - Patients (per million) treated with selpercatinib (all 19 tumor-types):
    - a) Commercial: 7.59 (year 1), 8.17 (year 2), and 8.76 (year 3).
    - b) Medicare: 36.29 (year 1), 39.08 (year 2), and 41.87 (year 3).
- Incremental PMPM estimates for years 1, 2, and 3 ranged from $0.073–$0.213 (commercial) and $0.371–$1.053 (Medicare) in the proxy comparator method, suggesting minimal impact of selpercatinib addition on payer budgets.
  - Findings based on the published literature costing for comparators were similar **(Figure 1 and 2)** in both perspectives.
- Most OWSA (across both perspectives and years) identified drug costs, incidence of *RET*, and Tx duration as significant drivers of incremental costs.
- *RET*-testing at 50% and GI-specific scenarios also had low number of patients treated and demonstrated minimal impact on payer budgets after addition of selpercatinib **(Table 3)**.
- These findings should be interpreted with caution given the uncertainty associated with several assumptions and parameters.

Key Assumptions and Limitations

- Plan size, annual incidence rate, and drug and AE costs do not change from the base year. Plan size does not affect the cost per person. All patients entered the model with 100% testing for *RET* and 100% were eligible for treatment. Assumptions of static populations, incidence rates, and costs were approximations to simplify the use of this iBIM; however, these are user-modifiable inputs.
- No Tx switching occurred in the model and that each year is independent of the next.
- For all included Tx in the model, an AE was included if ≥1 comparator reported the AE occurring in ≥5% in the published literature for any tumor type. AE rates were assumed as 0% if any Tx did not meet the 5% threshold.
- Infusion costs were obtained from the CMS.gov website. Medicare costs were converted to commercial values using an American Hospital Association's (AHA) Private to Medicare charge ratio (1.65) based on the average values from 2014-2018 before inflating costs to 2022. The AHA does not release average costs beyond 2018.[21,22]
- The BIM included ≥grade3 hospitalization costs and were assumed to be independent when there may have been either additional costs due to their severity or savings due to concurrent hospitalizations.
- The costs of grade 3 and grade 4 were not differentiated. The hospitalization costs were retrieved from the Healthcare Cost and Utilization Project (HCUP) website, which reports the mean cost associated with AEs identified by an ICD9/10 codes (converted to CCSR categories).[23]
- Base case drug Tx costs included WAC pricing from RED BOOK and since they do not include discounts, deductibles, or co-payments, they may not fully reflect the cost to a budget holder.
- Costs were truncated at 12 months, and the remainder were carried to subsequent years for those drugs with a duration of Tx >12 months.
- Inputs related to duration of Tx and AEs were extracted from individual publications based on clinical trials and not meta-analyses. These may differ from real-world clinical practice.

Acknowledgments and Disclosures

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