

THE COST-EFFECTIVENESS OF THERAPEUTIC DRUG MONITORING OF GENERIC IMATINIB FOR THE TREATMENT OF CHRONIC MYELOGENOUS LEUKEMIA

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INTRODUCTION

Many studies have demonstrated a correlation with imatinib mesylate (IM) blood levels > 1,000 ng/mL and response in chronic myelogenous leukemia (CML).¹⁻⁵ A blood level of 1,000 ng/mL has been recommended as the therapeutic target.⁶ A recent clinical study in CML used therapeutic drug monitoring (TDM) of IM to adjust doses so that blood levels in the personalized dosing arm reached the therapeutic range. The study found that the major molecular response (MMR) at 12 months was significantly improved with IM TDM compared to standard therapy without dose adjustment.⁷ Given that second generation tyrosine kinase inhibitors (TKI) had previously shown more rapid molecular responses at standard doses than imatinib, the improved IM efficacy using TDM provides new clinical information when selecting a CML treatment.

A recent cost-effectiveness analysis of TKI for CML found that, when considering the pending loss of patent exclusivity of IM, using IM as a first-line treatment is the most cost-effective treatment option where as physicians' choice of dasatinib or nilotinib was not cost-effective.⁸ However, since the loss of imatinib patent exclusivity in the US, no studies have considered the cost-effectiveness of IM with the loss of patent exclusivity, nor has the cost-effectiveness of IM TDM been evaluated.

OBJECTIVE

The objective of the study was to determine the cost-effectiveness of using generic IM TDM for the first-line treatment of CML.

METHODS

A peer-reviewed and published TKI cost-effectiveness model in CML⁸ was modified to include IM TDM as a treatment option. Efficacy inputs for major molecular response (MMR) rates were taken from published clinical studies: IM alone 37%, IM TDM 65%, dasatinib 52%, nilotinib 53%.^{7,9-11}

Using the Federal Supply Schedule (FSS) and average and lowest wholesale acquisition cost (WAC) as price bases, alternative estimates were used for drug prices including generic IM [Table 1]. The cost of TDM for IM was added to the IM TDM comparator arm at \$228 annually (6 tests at \$38 each) over 5 years. Other input costs from the Padula, et al. model were updated to 2016 U.S. Dollars using the Medical Service index of the Consumer Price Index.

The model compared two scenarios: (1) first-line IM TDM versus first-line IM alone, and (2) first-line IM TDM to first-line dasatinib or nilotinib. For the base case, it was assumed that half of the patients in the dasatinib/nilotinib arm received dasatinib and half received nilotinib as first-line treatment. As with the original model, for second-line TKI patients were assumed to switch once to a second-generation TKI in equal proportion in all comparator arms of the model.

The two scenarios outcomes were compared in terms of costs, quality-adjusted life-years (QALYs), and cost-effectiveness. A U.S. payer perspective was used with a 5-year time horizon and a 3.0% discount rate. Univariate (one-way) and multivariate (two-way) sensitivity analysis was performed on all key clinical and economic parameters.

TABLE 1: DRUG PRICE PER MG (\$/MG) AND REGIMEN ANNUAL COST SUMMARY* (\$)

Drug		FSS		WAC			
		Average		Low		Average	
		\$/mg	\$	\$/mg	\$	\$/mg	\$
Imatinib	Generic	0.12	13 406	0.39	43 963	0.59	65 848
	Brand	0.69	76 826	0.84	93 967	0.87	97 416
Dasatinib	Brand	2.47	68 721	2.88	80 091	4.20	116 868
Nilotinib	Brand	0.40	67 532	0.50	84 083	0.59	98 097

*Assuming 76.3% Adherence rate (source: Tsang, et al. Proc ASCO 2006, abst. 6119)

RESULTS

The model with the inclusion of IM TDM gave the following base case results for first-line treatment of CML:

- IM TDM is more cost effective than IM alone [Table 2].
 - IM TDM is a dominant treatment strategy (greater effectiveness and lower costs) versus IM alone.
 - Total cost savings with IM TDM ranged from \$15,452 with Average WAC pricing to \$36,940 with FSS pricing.
 - 0.25 QALYs were gained with IM TDM.
- IM TDM is more cost-effective than dasatinib/nilotinib [Table 3].
 - IM TDM is a dominant treatment strategy over dasatinib/nilotinib.
 - Total cost savings with IM TDM ranged from \$117,006 with Low WAC pricing to \$172,420 with FSS pricing.
 - 0.08 QALYs were gained with IM TDM.
- In a subgroup cost analysis of patients responding to IM TDM versus patients receiving first-line dasatinib/nilotinib, cost savings with IM TDM ranged from \$114,577 (WAC average pricing) to \$207,564 (FSS Average pricing) [Table 4].
- All results were confirmed as robust by univariate and multivariate sensitivity analyses.
- Key analysis included:
 - Given the uncertainty surrounding recent drastic price changes for imatinib, sensitivity analysis found that the base case pricing of generic imatinib could vary significantly before IM TDM is no longer dominant over dasatinib/nilotinib: 77% higher WAC low price, 58% higher WAC average price and 477% higher FSS price.
 - The MMR for IM TDM could decrease from a base case of 65% to 55% before IM TDM is no longer dominant over dasatinib/nilotinib, and it could drop to 38% before IM TDM is no longer dominant over IM alone,
 - Using either only dasatinib or only nilotinib in the dasatinib/nilotinib arm did not change the dominance of IM TDM over dasatinib/nilotinib,
 - Changes in the base case 3.0% discount rate did not change the dominance of IM TDM over IM alone and dasatinib/nilotinib.

TABLE 2: BASE CASE IM TDM & IM ALONE TOTAL COST (\$) AND QALY

Treatment	FSS Average	WAC		QALY
		Low	Average	
IM Alone	270 905	366 966	461 657	3.57
IM TDM	233 965	350 090	446 205	3.82
Difference	36 940	16 876	15 452	-0.25

TABLE 3: BASE CASE IM TDM VS. DASATINIB OR NILOTINIB TOTAL COST (\$) AND QALY

Treatment	FSS Average	WAC		QALY
		Low	Average	
Dasatinib or Nilotinib	406 385	467 106	575 606	3.74
IM TDM	233 965	350 090	446 205	3.82
Difference	172 420	117 016	129 401	-0.08

TABLE 4: BASE CASE IM TDM 5-YR. RESPONDERS VS. DASATINIB OR NILOTINIB TOTAL COST (\$)

Treatment	FSS Average	WAC	
		Low	Average
Dasatinib or Nilotinib	406 385	467 106	575 606
IM TDM	198 821	351 605	461 029
Difference	207 564	115 501	114 577

CONCLUSIONS

- Under a wide range of price scenarios as a first-line treatment for CML
 - IM TDM dominates IM alone,
 - IM TDM dominates dasatinib and nilotinib.
- A payor perspective analysis over 5 years demonstrated the potential of IM TDM to save hundreds of thousands of dollars.
- The analysis suggests that IM TDM is both a clinically and economically viable first-line treatment option for CML.

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