Frontline TKI Strategies for CML Patients: Balancing Outcomes and Costs in Pursuit of Treatment-Free Remission and Dose Reduction

Sanne JJPM Metsemakers[1], Rosella PMG Hermens[2], Geneviève ICG Ector[1], Nicole MA Blijlevens[1], Tim M Govers[3]

[1]Department of Hematology, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen, Netherlands
[2]Department of IQ Health, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen, Netherlands
[3]Department of Medical Imaging, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen, Netherlands

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Introduction

- Life expectancy of chronic myeloid leukemia (CML) patients approaches that of the general population by the advent of tyrosine kinase inhibitors (TKIs). CML, now a rare disease, will be one of the most common hematological malignancies in 2050 [1, 2].
- Imatinib has thus far been the most cost-effective frontline TKI [3, 4].
- CML management now includes dose reduction (DR) and treatment-free remission (TFR) to increase survival and limit adverse effects [1].

Objective

This unique model evaluates cost-effectiveness of all first and second-generation tyrosine kinase inhibitors for chronic myeloid leukemia incorporating treatment-free remission, dose reduction, upcoming second generation TKI cost reductions and older patients.

Methods

- A Markov model using 17 health states evaluates the most cost-effective frontline TKI for newly diagnosed adult CML chronic phase patients, incorporating TFR, DR, older patients, and second generation (2G) TKI patent expiration.
- Transition probabilities, costs and utilities were derived from literature data. Incremental cost-effectiveness ratios (ICERs) were calculated. Sensitivity analysis and model validation were conducted.

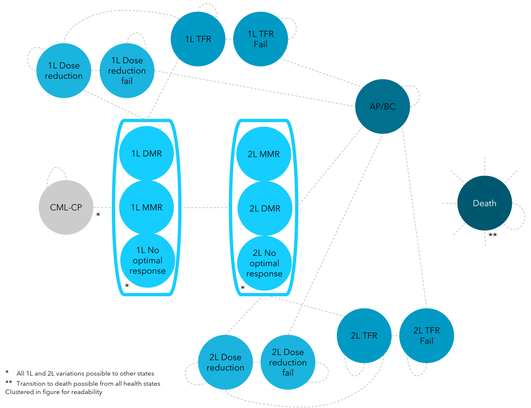

Figure 1 Conceptual Markov model with different health states after CML diagnosis including TFR and DR

Results

- Nilotinib is the most effective (20.13 QALYs) and imatinib is least effective (17.25 QALYs) in base case analysis including TFR and DR.
- Imatinib has a high probability of being cost-effective compared to dasatinib (89.80%), nilotinib (62.70%) and bosutinib (78.40%) at a WTP of €80,000/QALY.
- Without TFR and DR, fewer QALYs were generated. Bosutinib (20.05 QALYs) is most effective. Dasatinib (16.80 QALYs) and imatinib (15.93 QALYs) are least effective.
- For patients at age 70, imatinib has a high probability of being cost-effective compared to dasatinib (99.40%), nilotinib (93.60%) and bosutinib (97.80%).
- With a 50% 2GTKI cost reduction, nilotinib is considered cost-effective compared to imatinib (98.40%), dasatinib (94.80%) and bosutinib (68.90%).

Table 1 Base case results of the model including TFR & DR

Strategy	Costs (€)	Effects (QALY)	Comparator	Incremental costs (€)	Incremental effects (QALY)	ICER (€/QALY)
A: TKIs compared to Imatinib						
Imatinib	174,816.67	17.25	-			
Dasatinib	396,162.44	18.15	Imatinib	221,345.77	0.90	245,939.74
Nilotinib	427,395.49	20.13	Imatinib	252,578.82	2.88	87,700.98
Bosutinib	480,459.36	19.88	Imatinib	305,642.69	2.63	116,213.95
B: TKIs compared to Dasatinib						
Dasatinib			-			
Nilotinib			Dasatinib	31,233.05	1.98	15,774.27
Bosutinib			Dasatinib	84,296.92	1.73	48,726.54
C: TKIs compared to Nilotinib						
Nilotinib			-			
Bosutinib			Nilotinib	53,063.87	-0.25	Dominated by Nil

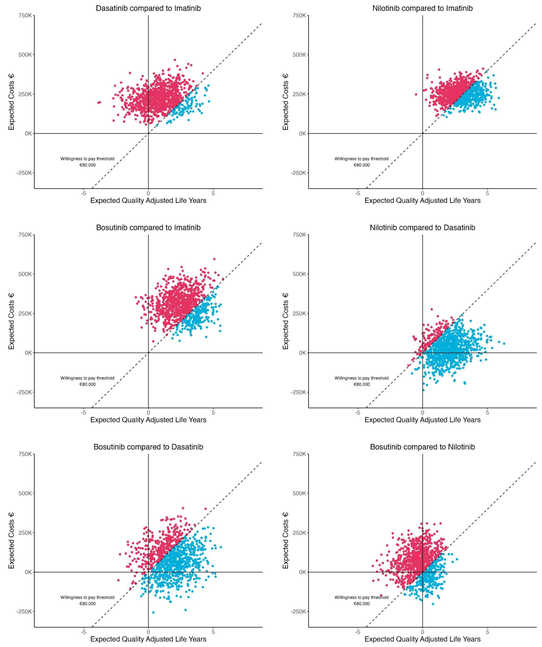

Figure 2 Incremental cost-effectiveness planes of model with TFR and DR

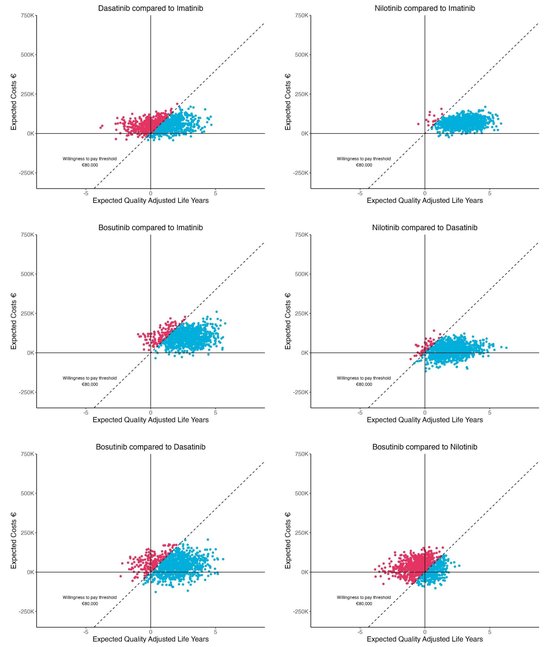

Figure 3 Incremental cost effectiveness planes of model TFR and DR and 50% 2GTKI cost reductions

Discussion

- Our model shows that the most effective strategy was nilotinib and the least effective strategy was imatinib, with a difference of nearly three years in full health.
- 2GTKIs generate more QALYs, also for older patients. However, with current TKI prices, imatinib remains cost-effective compared to 2GTKIs.
- As survival of CML patients has drastically improved, there is now an opportunity to shift focus towards improving QoL and reducing TKI-related toxicity. Including DR and TFR generates more QALYs, slightly increasing the probability of 2GTKIs being cost-effective.
- Cost reductions due to expected patent expirations of 2GTKIs greatly increase the probability of 2GTKIs being cost-effective.
- High-quality real-world data on newer TKIs, TFR and DR is necessary for further assessment of the applicability and successfulness of these treatment goals.

Implications for healthcare

Incorporating TFR and DR in the model substantially improves outcomes and reduces costs across all TKIs. This emphasizes the importance of adequate monitoring and strict guideline adherence to meet requirements for a TFR or DR attempt.

Cost reductions after patent expirations of effective 2GTKIs could increase worldwide availability of effective second-generation tyrosine kinase inhibitors.

Sanne Metsemakers, MSc
Department of Hematology
Radboud University Medical Center
Geert Grooteplein Zuid 8
Nijmegen, Netherlands
Sanne.Metsemakers@radboudumc.nl

LinkedIn

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Radboudumc university medical center