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ORIGINAL ARTICLE

Cost-effectiveness of dasatinib versus high-dose imatinib in patients with Chronic Myeloid Leukemia (CML), resistant to standard dose imatinib – a Swedish model application

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Abstract

Background. Chronic myeloid leukemia (CML) is a progressive disease, consisting of three phases, chronic, accelerated and blast phase. Treatment with imatinib has demonstrated high response rates and improved prognosis for patients with CML. The emergence of imatinib resistance is a major concern. Dasatinib is an oral kinase inhibitor of BCR-ABL that has been developed for treating CML patients across all phases of disease who are resistant or intolerant to imatinib. *Objectives.* The objective of this study was to assess the cost-effectiveness of dasatinib versus high-dose imatinib treatment in chronic phase CML patients, resistant to lower doses of imatinib (≤600 mg) in Sweden. *Methods and data.* A Markov simulation model was adapted to Swedish treatment practice. The model was populated with efficacy data from clinical trials, resource utilisation by expert opinion, published quality of life data and unit prices from official price lists. A life-long, societal perspective was used and sensitivity analyses were performed to test the robustness of the results. *Results.* The results showed that chronic phase CML patients resistant to standard dose imatinib gain on average 0.67 life-years, or 0.62 quality adjusted life-years, when treated with dasatinib 140 mg/day compared with high-dose imatinib 800 mg/day. The incremental societal cost amounts to EUR 4 250 during the lifetime period, or EUR6880 per QALY gained. *Conclusion.* The results indicate that dasatinib is a cost-effective treatment among imatinib-resistant CML patients in Sweden in comparison to imatinib 800 mg/daily.

Chronic myeloid leukemia (CML) is a malignant disease influencing blood cells and the third most common type of leukemia. Patients with CML have a specific identifiable marker called the Philadelphia (Ph) chromosome. CML is a progressive disease, consisting of three phases; the chronic phase (CP), which is the initial, usually stable phase of CML, the accelerated (AP) and blast phases (BP) both of which are considered as advanced CML. The quality of life is severely impaired during the final phases of the disease [1].

According to the Swedish CML registry with data from 2002–2006, the mean annual incidence in Sweden is estimated to be 0.9 per 100 000, or approximately 83 cases, with a median age of 58 years [2]. Furthermore, most patients (94%) are diagnosed in the CP whereas only 3% are diagnosed in the AP and BP, respectively.

The effectiveness of treatment for CML can be measured at the hematologic, cytogenetic and molecular levels. A hematologic response (HR) is measured by the amount of immature cells in a complete blood count after treatment. A HR can be complete (CHR) or partial (PHR). A cytogenetic response (CyR) after treatment is measured by the amount of cells with the Ph+ chromosome. A major cytogenetic response (MCyR) is defined as having ≤35% Ph+ cells (complete cytogenetic response [CCyR] = 0% Ph+ cells and partial cytogenetic response [PCyR] = 1 to 35% Ph+ cells). A molecular response (MR) is measured by the amount of BCR-ABL transcripts in the bone marrow or peripheral blood cells. A major molecular response (MMR) has been defined as a ≥3-log reduction in BCR-ABL transcripts. Deeper levels of response have been associated with improved prognosis in CML.

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Currently, a CyR is the surrogate marker of long-term disease control, as there is a strong relationship between CyR and survival [3,4].

Following Swedish recommendations, treatment with oral imatinib mesylate is considered first line treatment for patients with CML [1]. Treatment with imatinib has demonstrated high response rates and improved prognosis, especially in CP [5]. However, a major concern regarding the use of imatinib is the emergence of resistance [6]. It is estimated that around 20 to 30% of newly diagnosed patients with chronic-phase CML will require other treatment than standard therapy [7]. Studies have shown that high dose imatinib may be effective in some patients with resistance to standard dose imatinib and can improve response rates [8] but the responses seen are usually short-lived and durable response with imatinib is difficult to achieve [1,9]. Bone marrow transplant (BMT) still remains the only potential cure but only a small proportion of CML patients are eligible for a BMT procedure.

Dasatinib and nilotinib are oral kinase inhibitors that have been developed for treating CML patients across all phases of disease who are resistant or intolerant to imatinib [10,11], and therefore offers a treatment option for imatinib failure patients. Dasatinib has shown improved cytogenetic and molecular response rates and progression-free survival compared to high-dose imatinib [11]. Cost-effectiveness estimates of dasatinib treatment versus high-dose imatinib (800 mg) in CP-CML patients resistant to standard dose imatinib have been developed for Scotland, Austria and Spain [12–14]. Based on the fact that unit prices and clinical treatment patterns differ between countries cost-effectiveness results are expected to differ. The objective of this study is to evaluate the cost-effectiveness of dasatinib treatment versus high-dose imatinib (800 mg) in CP-CML patients resistant to standard dose imatinib in Sweden.

Methods and data

A Markov cost-effectiveness model with a probabilistic multivariate sensitivity analysis model was designed to calculate costs and effects associated with dasatinib treatment compared to high-dose imatinib among patients confirmed to be resistant to lower doses of imatinib (≤600 mg). The model is an adaptation to Swedish treatment practice from Taylor and colleagues [15]. It uses monthly cycles with probabilities for the likelihood of a health state change and all patients were assumed to start treatment in chronic phase (CP). The response to treatment after an initial 12-week treatment period determines the disease progression within the four health states; chronic phase (CP), accelerated phase (AP), blast crisis phase (BP) and dead (from either CML- or non-CML-related causes) (see Figure 1). Hence, the model is divided in a "within trial period" (months 1–3), and a "beyond trial period" consisting of a medium term (months 4 to 12) and a long term (months 13 and onward). At each monthly cycle, the patient faces a probability of staying in the same health state or moving to the next. It is not possible to move from CP to BP directly, whereas the probability of CML-related death is dependent on the health state and the treatment response of the patient. Age-specific annual non-CML-related mortality rates are derived from Statistics Sweden [16].

The results from the analysis are expressed in incremental cost per quality-adjusted life years (QALY) gained. In the base case analysis the study population is patients resistant to imatinib with a starting age of 60 years which is in line with Swedish clinical practice. In line with Swedish guidelines both costs and benefits are presented with a lifetime societal perspective and discounted by 3% per year [17].

Clinical data

Response to treatment data is taken from a 12 week head-to-head clinical trial including 150 patients in chronic phase resistant to conventional doses (400–600 mg) of imatinib [11]. Resistance was defined as any of: 1) a rising white blood cell count after the initiation of treatment with imatinib, 2) a failure to achieve complete haematological response (CHR) after three to six months of imatinib therapy, 3) a loss of CHR at any time under therapy, 4) a failure to achieve major cytogenetic response (McyR) after 12 months of therapy, 5) a loss of MCyR at any time during therapy. Patients were randomised to receive either of two treatment therapies: dasatinib

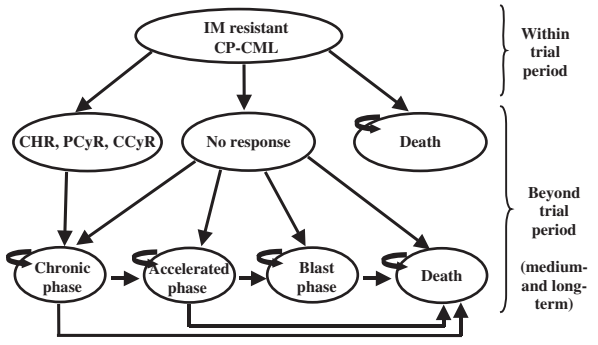

Figure 1. Markov model structure starting with imatinib (IM) resistant chronic phase (CP-CML). CHR = complete haematological response; PCyR = partial cytogeneticresponse; CCyR = complete cytogenetic response.

140 mg per day (101 patients) or imatinib 800 mg per day (49 patients). The median age was 51 years and approximately 50% of the patients in the dasatinib group and 20% in the imatinib groups were male. The median disease duration for the dasatinib and imatinib groups was 64 and 52 months respectively (for full details in patient characteristics see [11]).The best response achieved at the end of the 12 week trial period is presented in Table I. The table should be interpreted as 7.9% (18.4%) of patients with no response to dasatinib (imatinib) in CP has a probability of remaining in CP the next month of 0.831 or moving to AP of 0.169. In the next cycle (month) patients remaining in CP are exposed to the same probabilities. Patients in AP, however, now move to the next row and face a probability of 0.826 of remaining in AP, moving to BP or death (probabilities 0.124 and 0.05, respectively). Hence, the better initial response (CCyR > PCyR > CHR), the slower the expected cohort disease progression. The progression data is taken from published literature [3,4,18,19].

Utility data

Utility weights for each health state were elicited with a time-trade-off (TTO) technique using the EQ-5D instrument among 100 lay persons in the UK (Table II), and applied both to the imatinib and dasatinib arms [20]. The variation around the mean is used in the probabilistic sensitivity analysis. In the sensitivity analysis we use utility weights provided for a NICE appraisal of imatinib [21] (Table II).

Costs

The Swedish treatment practice was elicited from interviews with two Swedish clinical haematologists at the same facility. The resource utilisation, and unit costs in EUR 2008, are presented in Table II and describes the average number of resources used per patient and month in each health state. Direct health care related unit costs for pharmaceuticals and other health care resources are included [22,23]. Costs for study medication are added each month that a patient is still in the chronic phase. The inpatient cost corresponds to a bed day at a haematological clinic plus one haematologist visit per day. Any other services such as treatment, diagnostic or surgical procedures are not included. The cost for thrombocyte transfusion is based on a regional cost-per-patient-study inflated to year 2008 by CPI. The variation around the unit costs for the probabilistic sensitivity analysis is taken from four Swedish university hospitals' fees (Lund, Göteborg, Linköping, Umeå) for haematologist visits and tests (coefficient

Table I. Initial best response within trial and monthly progression rates beyond trial period.

	Initial best response (11)		Probability of being in the health state month 4–12				Probability of being in the health state month 13+			
Initial response rate	Das	Im	CP	AP	BP	Death	CP	AP	BP	Death
No Response										
Chronic phase (CP)	7.9%	18.4%	0.831[a]	0.169[d]	0.000[b]	0.000[b]	0.831	0.169[d]	0.000[b]	0.000[b]
Accelerated phase (AP)	n.a.	n.a.	0.000[b]	0.826[a]	0.124[e]	0.050[e]	0.000[b]	0.833[a]	0.124[e]	0.043[e]
Blast phase (BP)	n.a.	n.a.	0.000[b]	0.000[b]	0.826[a]	0.174[e]	0.000[b]	0.000[b]	0.926[a]	0.074[e]
CHR										
Chronic phase (CP)	57.4%	53.1%	0.993[a]	0.007[c]	0.000[b]	0.000[b]	0.980	0.020[f]	0.000[b]	0.000[b]
Accelerated phase (AP)	n.a.	n.a.	0.000[b]	0.977[a]	0.006[e]	0.017[e]	0.000[b]	0.943[a]	0.038[e]	0.018[e]
Blast phase (BP)	n.a.	n.a.	0.000[b]	0.000[b]	0.941[a]	0.059[e]	0.000[b]	0.000[b]	0.977[a]	0.023[e]
PCyR										
Chronic phase (CP)	13.9%	20.4%	0.997[a]	0.003[c]	0.000[b]	0.000[b]	0.994	0.006[f]	0.000 [b]	0.000[b]
Accelerated phase (AP)	n.a.	n.a.	0.000[b]	1.000[a]	0.000[e]	0.000[e]	0.000[b]	0.962[a]	0.022[e]	0.016[e]
Blast phase (BP)	n.a.	n.a.	0.000[b]	0.000[b]	0.941[a]	0.059[e]	0.000[b]	0.000[b]	0.964[a]	0.036[e]
CCyR										
Chronic phase (CP)	20.8%	8.2%	0.997[a]	0.003[c]	0.000[b]	0.000[b]	0.995	0.005[f]	0.000[b]	0.000[b]
Accelerated phase (AP)	n.a.	n.a.	0.000[b]	1.000[a]	0.000[e]	0.000[e]	0.000[b]	0.995[a]	0.002[e]	0.003[e]
Blast phase (BP)	n.a.	n.a.	0.000[b]	0.000[b]	0.985[a]	0.015[e]	0.000[b]	0.000[b]	0.989[a]	0.011[e]

Legend: CHR = complete haematological response; PCyR = partial cytogenetic; CCyR = complete cytogenetic; n.a. = not applicable; Das = dasatinib; Im = imatinib.
Sources: [a]Residual probability; [b]Assumption; [c]Kantarjian [4]; [d]Holowiecki [18]; [e]Aoki [3]; [f]Silver [19].
Note: Only patients in CP receive study drugs why initial best response is only applicable for CP. Deaths from CML and natural causes have been collapsed.

Table II. Input data: utility weights, resource use per month and unit cost reflecting Swedish treatment practice (EUR2008).

	Resource use per month*					
Resource item	CP Responder	CP Non-resp.	AP	BP	Unit cost (SD)	Source
Haematologist visit	0.33	1.00	2.00	2.00	184 (75)	(23)
Inpatient stay	0.00	0.00	0.17	0.42	541 (222)	(23)
Chest x-ray	0.00	0.00	0.33	0.50	56 (8)	(23)
CT scan	0.00	0.00	0.08	0.08	220 (31)	(23)
Bone marrow test	0.33	0.33	0.33	0.33	784 (110)	(23)
Cytogenetic testing	0.33	0.33	0.33	0.33	365 (51)	(23)
PCR test	0.33	0.08	0.00	0.00	655 (92)	(23)
Other laboratory tests	1.50	2.00	2.00	4.00	14 (2)	(23)
Thrombocyte transfusion	0.00	0.00	0.63	2.50	914 (375)	(23)
Imatinib 800 mg/day (monthly cost)					4 869	(22)
Dasatinib 140 mg/day (monthly cost)					4 239	(22)
Monthly production loss (85% activity)					3 830	(24)
Public consumption age 50–64					1 461	(25)
Public consumption age 65–74					1 465	(25)
Public consumption age 75–84					1 678	(25)
Public consumption age 85–					2 514	(25)
Utility weights						
Base case	0.90	0.72	0.53	0.29		(20)
	CI: 0.87–0.93	CI: 0.67–0.77	CI: 0.48–0.57	CI: 0.24–0.34		(21)
One-way sensitiv analysis	0.85	0.85	0.73	0.52		

Note: *Based on expert opinion.

of variation 41% and 14% respectively), assuming a Gamma distribution. This variation is intended to reflect the geographic variability in treatment costs. The average monthly salary for individuals aged 45–64 years including pay-roll taxes of 41% is used for estimating the indirect cost in terms of production loss (human capital approach) [24]. We assume 85% work force participation among CML patients <65 years, recommended by the clinical experts as not all patients are on the labour market for other reasons than the CML diagnosis. According to the Swedish guidelines on economic evaluations the costs for increased survival – total consumption less total production during gained life years – should be included if the treatment affects survival [17,25]. Therefore we include the expected increase in public consumption due to extended survival resulting from either treatment in the analysis.

Adverse events

Disutility weights for adverse events related to the regimens are lacking. We have therefore limited the inclusion of treatment-related costs for adverse events to the sensitivity analysis and it is assumed that the patient continues with the study medication. Adverse event rates related to the regimens are taken from the clinical trial and applied only to the first month as we have no data on long term event rate (Table III) [11].

Sensitivity analysis

Several one-way sensitivity analyses are performed (base case in parenthesis):

1. time horizon 10 years (lifetime),
2. discount rate 0% (3%),
3. inclusion of adverse event (AE) costs (not included),
4. patients intolerant to imatinib (patients resistant to imatinib), and
5. utility weights provided for a NICE appraisal of imatinib [21] (TTO among CML-patients).

The variation in effects in terms of both initial response and utilities, as well as direct costs, except for the study medication, are included in the probabilistic sensitivity analysis. We used beta and gamma distributions for probabilities and costs, respectively. The results from 1 000 cohort iterations are presented as a scatter plot in the incremental cost-effectiveness plane. In the plot we have also added the estimated willingness-to-pay for a QALY in Sweden of SEK 655 000 (EUR 68 190) as a full straight line, although no formal threshold value exists. This value is derived from the willingness-to-pay of preventing a traffic fatality in Sweden [26].

Results

In the base case analysis with a lifetime perspective, patients resistant to standard dose imatinib in the

Table III. Sensitivity analysis: probabilities and unit costs for adverse events in the first month of treatment (EUR, 2008).

Adverse events	CP	AP	BP	Unit cost
Diarrhoea (dasatinib)	0.02	0.06	0.07	184[a]; 2 865[b]
Diarrhoea (imatinib)	0.02	0.02	0.02	
Headache (dasatinib)	0.02	0.01	0.00	184
Headache (imatinib)	0.02	0.02	0.02	
Fatigue (dasatinib)	0.01	0.04	0.01	184
Fatigue (imatinib)	0.04	0.04	0.04	
Thrombocytopenia (dasatinib)	0.23	0.13	0.13	
Thrombocytopenia IM	0.08	0.08	0.08	
Dyspnoea (dasatinib)	0.03	0.04	0.05	240
Neutropaenia (dasatinib)	0.00	0.00	0.11	3 530
Pleural effusion (dasatinib)	0.02	0.02	0.12	885

Notes: CP: chronic phase; AP: accelerate phase; BP: blast phase; Non-resp.: non-responder to treatment in chronic phase; [a]Chronic phase, [b]Accelerated or blast phase.

chronic phase gain on average 0.67 life-years, or 0.62 quality adjusted life-years, when treated with dasatinib 140 mg/day compared with high-dose imatinib 800 mg/day (Table IV). The incremental societal cost amounts to EUR 4 250 during the lifetime period, or EUR 6 880 per QALY gained. As seen in Table IV the indirect costs in terms of production losses and increased public consumption due to decreased mortality, almost cancel out.

Of the direct health care related costs, the medication accounts for almost 80% in both treatment arms. Patients treated with dasatinib generate higher other direct health care costs as a result of the extended life expectancy during which more resources for tests and procedures are accumulated. In particular bone marrow examinations (cytology and cytogenetics) and PCR tests constitute the largest incremental cost items with four tests per year each. On the other hand, the cost for thrombocyte transfusions falls due to a shorter duration of the blast phase among dasatinib treated patients where transfusions are most frequent (2.5 per month). When accounting for only direct costs, the incremental cost-effectiveness ratio is estimated to EUR 7 207 per QALY gained.

Table IV. Base case analysis: societal and lifetime perspective, imatinib 800 mg/day vs dasatinib 140 mg/day, discount rate 3% (EUR, 2008 prices).

Cost item	Dasatinib	Imatinib	Difference
Treatment (drug)	277 778	278 210	–432
Specialist visits	8 063	7 734	329
Inpatient stay	1 916	1 963	–48
Imaging and blood tests	2 254	2 113	140
Bone marrow tests	19 791	17 703	2 088
Cytogenic tests	9 219	8 247	972
PCR Test	14 133	12 320	1 813
Thrombocyte transfusions	17 806	18 217	–411
Total direct cost	**350 960**	**346 507**	**4 452**
Production losses	41 834	53 826	–11 991
Increased public consumption	111 738	99 948	11 789
Total societal cost	**504 532**	**500 281**	**4 250**
Life years (LY)	6.37	5.69	0.67
QALYs	5.19	4.57	0.62
Incremental societal cost/LY		6 332	
Incremental societal cost/QALY		6 880	

The estimated disease progression for the dasatinib and imatinib cohorts are presented in Figure 2. Patients progress from the chronic phase to the accelerated and blast phases, and to death. After ten years almost 22% of the dasatinib patients are estimated to still be in the chronic phase, or 3.4 percentage points more than in the imatinib arm. At the same time almost 4 percentage points more patients are alive in the dasatinib arm compared to the imatinib arm and, therefore, continue to consume health care and other resources.

Sensitivity analysis

In the one-way sensitivity analysis (Table V), dasatinib is a dominant treatment option, i.e. generating both cost savings and more health, in a 10-year time perspective (analysis 1), in which costs and effects are accumulated up to the age of 70. As the official retirement age in Sweden is 65 years, the reduced production losses with dasatinib outweigh the increased public consumption (EUR 3 686, data not shown) resulting from increased survival. Consequently, when adopting a societal perspective where both production gain and increased public consumption resulting form survival gains, a lower age of the patient would increase the potential cost offset with dasatinib treatment, and *vice versa*. A zero discount rate (analysis 2) in a life-long time perspective increases the incremental cost to EUR 11 075 (160%) whereas the QALYs gained increases to 0.79 (27%), indicating that long-term survival is important for

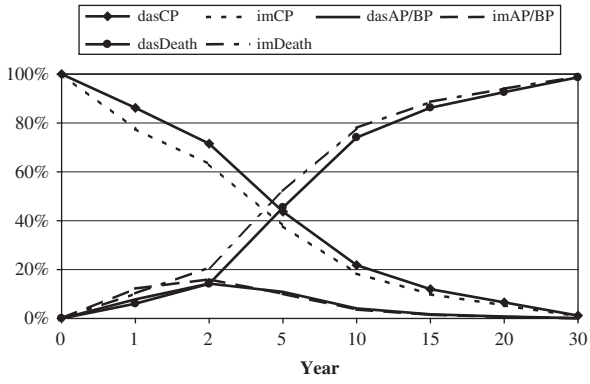

Figure 2. Distribution of patient cohort in each health state over time (%) at the beginning of each year. das = dasatinib; im = imatinib; CP = chronic phase; AP/BP: accelerated and blast phases.

costs. The inclusion of AEs in sensitivity analysis 3 is motivated by the uncertainty around the probabilities for experiencing AEs, and the fact that health effects associated with AEs, i.e. disutilities are not accounted for in the model. The inclusion of AE affects costs very little (EUR 46). For patients intolerant to imatinib, dasatinib may be the only available treatment alternative. Hence, comparing dasatinib to no study treatment, i.e. all patients are "non-responders", generates 6.4 QALY gained to a cost of almost EUR 450 500 (analysis 4). The utility weights in the sensitivity analysis 5 are more conservative than those used in the base-case as there is no quality of life difference between responders and non-responders to treatment in the chronic phase. However, the impact of this set of utility weights on the ICER is very small.

The probabilistic sensitivity analysis that restricts costs to direct CML-related health care costs only shows a rather great variation in both costs and effects when introducing uncertainty around the input parameters. In Figure 3, the mean incremental cost and QALY gain amount to EUR 4 330 and 0.63, respectively, or 6 869 EUR/QALY. The incremental costs are scattered on both sides of the X-axis, indicating that dasatinib can generate cost-savings (43% observations below X-axis). Two percent of the observations are located to the left of the Y-axis, indicating observations where the QALY gain is higher for imatinib. Hence, according to the probabilistic sensitivity analysis it could be expected that dasatinib generate more health in terms of QALYs gained, but it is uncertain whether this health benefit comes at an extra cost or if it generates cost-savings. However, there is a clear relationship between incremental survival and incremental costs, since greater life expectancy carries a healthcare burden due to greater exposure to resource utilisation. As seen, all observations fall below the derived willingness-to-pay for a QALY in Sweden (full straight line) indicating that dasatinib treatment would be cost effective if the willingness-to-pay for avoiding a traffic fatality is the same for the health care sector.

Table V. One-way sensitivity analysis of dasatinib 800 mg/day vs. imatinib 140 mg/day (EUR, 2008 prices).

Parameter change	Incremental cost	QALY gained	ICER
Base case	4 250	0.62	6 880
1. 10-year perspective	–4 212	0.45	Dominant
2. Discount rate: 0%	11 075	0.79	13 981
3. Including costs for adverse event	4 296	0.62	6 955
4. Imatinib intolerant patients	450 416	6.40	70 335
5. Utility weights from imatinib study [21]	4 250	0.58	7 322

Note: Dominant indicates that dasatinib is both cost-saving and generates more health benefits than imatinib.

Discussion

We found that dasatinib is a cost-effective treatment option compared to high-dose imatinib in patients resistant to standard dose imatinib. Similar results were seen in Scotland, Austria and Spain using the same model [12–14]. These studies resulted in cost-savings of GBP 10 579 and EUR 15 213, respectively. The main difference from our results is the exclusion of indirect cost (corresponding cost per QALY gained is EUR 7 207 in Sweden), but also different starting ages, discount rates, life expectancies, unit prices and resource use. This indicates the importance of nationally adapted analyses to accommodate for differences in treatment practice, unit costs and health economic guidelines.

There are some limitations with this model analysis. First and foremost, the small number of patients diagnosed with CML annually makes it difficult to obtain reliable data and information on treatment practice in less common phases such as the accelerated and blast phases. Experts thus find it difficult to accurately estimate the resource consumption in spite of their long haematological experience with CML treatment in Sweden, but we argue that it is the best available information for the time being. Furthermore, the long-term results in this study have been made on estimations based on fairly short-term studies. This is a common problem in modelling studies, especially in the early phase of a product's life cycle as no long-term data is available. The sensitivity analysis is therefore important to address some of the uncertainties regarding the results' validity when extrapolating costs and effects.

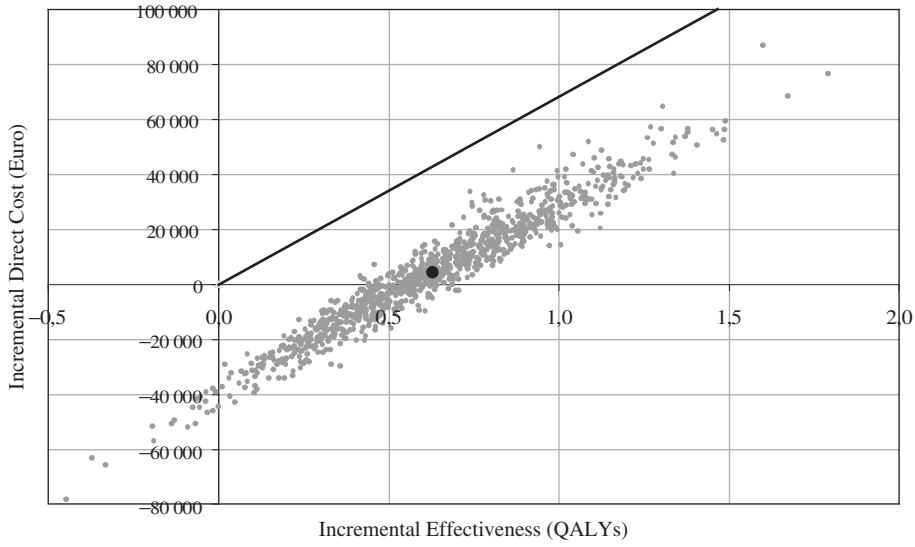

Figure 3. Incremental cost-effectiveness plane of dasatinib vs imatinib. Note: the straight line indicates an estimated willingness-to-pay for a QALY in Sweden [23].

Nevertheless, models are important tools for *ex ante* decisions and are easy to update as more information becomes available.

In the clinical trial of dasatinib *versus* imatinib the mean study patient age was 51 among patients in chronic phase failing imatinib ≤600 mg daily. In our base case analysis we use a starting age of 60 as this age is considered to be more representative from a Swedish clinical perspective and the resource consumption was estimated for this patient population. However, as the prognosis of the patients, as well as the resource consumption, may be age-dependent in Sweden it is unclear whether the efficacy of dasatinib over imatinib freely translates to other age cohorts. However, the model is constructed on a "head-to-head" clinical trial so that the two study arms are comparable, and we do not suspect any bias in the results due to differences in the patient population why we consider it to be more relevant to choose a starting age of 60 years. Furthermore, we have assumed identical utilities for both study medications, which may not be the case given potential differences in for example adverse event profiles or maintenance of response.

Another potential limitation with the model design is that it does not allow for an absorbing health state for bone marrow transplantations (BMT) for those patients who would be considered relevant for this. Including BMT as a separate health state would probably result in a higher cost in the imatinib arm as more patients experience treatment failure in the imatinib arm, thus undergoing BMT to a higher extent. These patients could then be expected to have an extended survival during which indirect costs would be accumulated. As both costs and effects could be expected to increase in the imatinib arm, the net effect on the incremental cost-effectiveness is therefore uncertain. Alternatively, it may be possible that the improved response rates observed in the dasatinib arm result in a greater number of patients becoming eligible for BMT, or increasing their probability of success if a BMT is undertaken. Such data are not yet available and, therefore, this option was excluded from the model.

Results from a study investigating dose-optimisation of dasatinib for imatinib-resistant or intolerant CP-CML patients concluded that 100 mg dasatinib once daily retains the efficacy of 70 mg twice daily but with improved tolerability [27]. This more favourable dose regimen is also the Swedish treatment practice today. The acquisition cost for dasatinib is identical, however, and the change in treatment practice may therefore have a positive impact on the cost-effectiveness results as a lower dasatinib dose can reduce the adverse events and the associated costs.

Nilotnib is approved for treatment of chronic phase and accelerated phase CML in adults resistant to or intolerant to imatinib. To our knowledge, there are neither clinical head-to-head studies comparing dasatinib and nilotinib nor any cost-effectiveness studies to compare our results with. Although health economic models allow indirect comparisons with different treatment alternatives, direct comparisons have a higher validity in the clinical results. We therefore do not want to include an indirect analysis in this study as the quality of the clinical input data could differ between the analyses, leading to difficulties in conclusions.

Conclusions

The results indicate that dasatinib treatment in CML patients resistant to standard dose imatinib in Sweden is a cost-effective treatment in comparison to imatinib 800 mg/daily. Dasatinib is expected to generate greater health benefits at a cost per QALY of about EUR 6 880 with a life-long societal perspective.

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