Appendix 11

Summary of the included economic analysis and economic evaluation studies

Study identification	Author and year	Chabot 2008[95]
	Intervention studied/ comparators	BSC vs sunitinib for imatinib-resistant or -intolerant patients
	Hypothesis/question	Examine the challenges to undertake cost-effectiveness study in oncology using crossover trial, and presented the submission to the CDR of a cost-effectiveness evaluation of sunitinib vs BSC for treatment of GIST in patients who are imatinib resistant or intolerant
Key features of the study	Type of study	Descriptive, and a full economic evaluation (cost-effectiveness analysis)
	Target population/sample population	Patients who failed or are intolerant to imatinib
	Context/settings	Canada, hypothetical population at provincial level
	Date to which the data of the study relate	2005
	Source of effectiveness data	Clinical effectiveness from Phase III clinical trials (NCT00075218)[52] Health outcome – QALY-based utility measured by EQ-5D questionnaire administered on clinical trial patients
	Modelling	Markov modelling
	Link between effectiveness and costs data	Costs in the model include costs of sunitinib acquisition, and health-care resource use for BSC, cost of routine follow-up for patients receiving sunitinib, cost of adverse events, and end-life costs. Information on health-care resource use and corresponding unit costs were derived from published literature, medical oncologist and Canadian Government Schedule
Information on the clinical evidence and effectiveness – main outcome of the study	Sample patients/study sample/ patient groups	Cohort population in the model
	Study design	Modelling for cost–utility analysis
	Effectiveness analysis	The following trial end points were used for the valuation of the outcomes (effectiveness): (a) PFS, defined as the time from randomisation to the point when the tumour progressed or death was due to GIST (b) OS (c) utility, measured by the EQ-5D (d) treatment-related adverse events

	Effectiveness measures and results/outcome measures	Sunitinib compared with BSC for the patients who failed or did not respond to imatinib and found sunitinib more effective than BSC – in terms of OS, PFS, LYG, LYS and QALY
	Primary end points/outcome and secondary end points/outcome	Mean survival sunitinib group,1.6 years; mean progression-free health state, 0.5 years; and 1.1 years with PD
		Patients in BSC group spent on average 0.2 years in the progression-free health state and 0.7 years with PD; and had mean survival of 0.9 years
		Sunitinib treatment resulted in 0.7 LYG, and 0.4 QALYs compared with BSC
	Statistical precision of these outcomes	Utilities associated with sunitinib:
		No progression during 4 weeks' sunitinib: 0.712 ± 0.2
		Next 2 weeks' utility improvement: 0.081 ± 0.02
		No progression BSC: 0.781 ± 0.2
		Progression: $0.577 + 0.3$
	Clinical recommendations and conclusion	The initial CDR recommendation based on the economic evaluation was 'not to reimburse' sunitinib in Canada. This was reversed owing to the fact that patients who are resistant to imatinib have no other treatment options. Based on review of the quality, safety and efficacy data, Health Canada concluded that sunitinib had favourable risk–benefit profile for the treatment of GIST after failure or intolerance of imatinib treatment
Economic analysis	Measures of health outcome/ benefits used in the economic analysis	QALY based on EQ-5D from UK study[55]
	Direct costs and its components	*Cost per 6-week cycle*
	Prospective or retrospective (depend on study design)	Sunitinib treatment standard dose: C$6947.99
	Whether values were imputed in for certain cases	Sunitinib treatment reduced dose for adverse event management: C$5210.99
	How hospital stay was defined, and whether any classifications were used or not	Sunitinib treatment medical follow-up: cycle 1 C$2275.13, cycle 2 726.47, cycle 3+ 1072.11
	Costing of complications or side effects	Terminal phase – end-of-life cost C$3752. Cost of serious adverse event with sunitinib $42.84
	Estimations of unit costs and source/methods	
	Indirect costs and its components	
	Cost of productivity, cost of volunteer care and support for the patient	Not considered
	Currency, year prices	C$, at 2005 prices
	Statistical analysis/cost	Mean and standard deviation of the progression and progression-free time
	Sensitivity analysis	Univariate sensitivity analysis was conducted by varying the most influential model parameters, namely utility of progression and no progression, OS (HR), PFS, PET at initiation of sunitinib treatment, the cost of palliative care and the cost of PET. The model assumed the cost of acquisition of sunitinib is certain and did not vary this in sensitivity analysis. The sensitivity analysis suggests that results of the economic evaluation were most sensitive to health-state utility value and rate of OS and PFS

Results/major findings	Benefits results from the economic evaluation	Mean QALYs: Sunitinib 0.97 BSC 0.54 ICER ($/LYS) 49,826 ICUR ($/QALYs) 79,884 These (ICER, ICUR lies between an estimated thresholds boundary of $26,433–132,166)
	Costs results used in the economic evaluation	*Mean costs in C$*
	Cost of treatment, costs to health sector (cost to NHS)	Sunitinib $46,125 BSC $11,632
	Major determinants of costs, the principle costs drivers	
	Synthesis of costs and benefits	*Cost-effectiveness of sunitinib vs BSC*
	Any attempt to consider the uncertainty surrounding estimates of effects	ICER ($/LYS) 49,826 ICUR ($/QALYs) 79,884 Sensitivity analysis – sensitivity uncertainty in the OS advantage for sunitinib? As patients were allowed to cross over
	Author conclusion/ recommendations	Sunitinib cost-effective The decision of approval for sunitinib from Health Canada was based on the recognition of sunitinib's clinical benefits for the imatinib-intolerant group. The paper suggests reliance on cost-effectiveness methodology is unsatisfactory Guidance is needed on how better to reconcile the best available clinical trial data with the cost-effectiveness requirements and the objectives of prompt access to oncology medicine

CDR, Canadian Drug Review; ICUR, incremental cost–utility ratio.

Study identification	Author and year	Contreras-Hermandez 2008[96]
	Intervention studied/ comparators	Sunitinib 50 mg/day, imatinib 800 mg/day and BSC
	Hypothesis/question	Examine the cost-effectiveness to compare the alternatives (imatinib 800 mg/day, sunitinib 50 mg/day) as second line of treatment for those who failed or became intolerant with imatinib 400 mg/day. The study examined whether it is worth it for the Mexican insurance system to reimburse for sunitinib or higher dose of imatinib
Key features of the study	Type of study	Model-based (Markov) full economic evaluation (cost-effectiveness analysis)
	Target population/sample population	Twenty-one advanced GIST patients who were treated at Hospital de Oncología IMSS, Mexico. Treatment examined over 5 years
	Context/settings	Mexico, 21 advanced GIST patients who were treated at Hospital de Oncología IMSS
	Dates to which the data of the study relate	January 2005 to 31 December 2007
	Source of effectiveness data	Clinical trial and published literature Motzer *et al.* 2006[104] – sunitinib Phase III study and study by Demetri *et al.* 2006[52] mainly from survival data and 21 advanced GIST patients who were treated at Hospital de Oncología IMSS
	Modelling	Markov model. Model utilised the effectiveness data from Motzer *et al.* 2006[104] (review of sunitinib treatment) – sunitinib Phase III study and study by Demetri *et al.* 2006[52]
	Link between effectiveness and costs data	All costs used in the model (except for the cost of sunitinib) were based on the information from IMSS pricing and reimbursement procedures. For cost of sunitinib, as it was not available in the Mexican market at the time of the analysis, the cost information was provided by Pfizer Laboratories. Costs included cost of mean number of visits to the oncologist, laboratory examinations, and radiology procedures, and cost of mean length of stay

Information on the clinical evidence and effectiveness, main outcome of the study	Sample patients/study sample/patient groups	Twenty-one advanced GIST patients who were treated at Hospital de Oncología IMSS and hypothetical cohort of 1000 patients for modelling exercise
	Study design	Observation study based on 21 patients and Markov modelling with a follow-up period of 5 years
	Effectiveness analysis	PFMs, PFS, LYG
	Effectiveness measures and results/outcome measures	
	Primary end points/outcome and secondary end points/ outcome	PFMs 5.64 and 1.4 LYG (95% CI 1.3 to 1.6) for sunitinib
		Imatinib – PFM = 5.28 and 1.31 LYG (95% CI 1.1 to 1.4)
		BSC – PFM = 2.52 and 1.08 LYG (95% CI 1.0 to 1.3)
	Statistical precision of these outcomes	
	Clinical recommendations and conclusion	Sunitinib as second line of treatment for those who failed with 400 mg
Economic analysis	Measures of health outcome/ benefits used in the economic analysis	PFMs
		LYGs
	Direct costs and its components	Direct costs estimated from treatment follow-up, health systems perspective
		Imatinib higher dose: expected costs per patient US$35,225 (SD US$1253)
		Sunitinib: expected costs per patient US$17,805 (SD US$694.83)
		BSC: expected cost per patient US$2071.86 (SD US$472.88)
		Using IMSS data, the estimated annual cost per patient for medical consultation, hospitalisation, laboratory examination and radiology procedures was $2424.32, $2657.57, $566.99 and $2392.67, respectively
	Indirect costs and its components	
	Cost of productivity, cost of volunteer care and support for the patient	Not taken into consideration
	Currency, year prices	US$, at 2006 prices
	Statistical analysis/cost (whether parametric or non-parametric bootstrap used to generate the CIs around each difference in costs and differences in total costs	Standard deviation of the mean costs, and mean life-years saved, and CI of the mean life-years saved
	Sensitivity analysis: one way or two way	Monte Carlo second order sensitivity analysis, probabilistic sensitivity analysis conducted
		Results from the sensitivity analysis were used to develop the acceptability curve
Results/major findings	Benefits results from the economic evaluation	Sunitinib resulted in mean PFMs of 5.64, and 1.4 LYG
		For imatinib, PFM = 5.28, and 1.31 LYG
		For BSC, PFM = 2.52, and 1.08 LYG
		Incrementally, sunitinib yielded 0.32 LYG when compared with BSC
		ICER: sunitinib vs BSC
		$15,734.23 per patient treated with sunitinib and $56,612.55 per year of PFS and $46,108.89 per LYG
	Costs results used in the economic evaluation	Imatinib higher dose: expected cost per patient US$35,225 (SD US$1253)
		Sunitinib: expected cost per patient US$17,805 (SD US$694.83)
		BSC: expected cost per patient – US$2071.86 (SD US$472.88)
		Using IMSS data, the estimated annual cost per patient for medical consultation, hospitalisation, laboratory examination and radiology procedures was $2424.32, $2657.57, $566.99 and $2392.67, respectively
	Author conclusion/ recommendations	Reimbursing sunitinib over high dose of imatinib would deliver cost savings to the IMSS and greater survival benefits

IMSS, Instituto Mexicano del Seguro Social.

Study identification	Author and year	Mabasa 2008[98]
	Intervention studied/ comparators	Imatinib vs no imatinib (BSC) in GISTs
	Hypothesis/question	Examine the cost-effectiveness of imatinib
Key features of the study	Type of study	Full economic evaluation (cost-effectiveness analysis)
	Target population/sample population	Patients in British Columbia, BCCA patients with advanced GIST who received imatinib or historical treatment
	Context/settings	BCCA-registered patients with advanced GIST, British Columbia, Canada
	Dates to which the data of the study relate	1996–2001 for non-imatinib cases 2002–5 imatinib cases. Follow-up periods: 60 months and 44 months, respectively
	Source of effectiveness data	Data derived from medical records of the patients
	Modelling	No modelling, patient-level data used for CEA
	Link between effectiveness and costs data	All costs used were based on the information on the BCCA patients followed and included on an intention-to-treat basis. The mean and median duration of follow-up for the imatinib group were significantly longer than for the historical group Costs of treatment include cost of drugs, cost per cycle of 1 month, cost of labour and supply (not clearly specified what it includes) and cost of counselling Costing was based on BCCA registry: ■ ICER imatinib vs no imatinib per median LYG (incremental cost per LYG) ■ ICER imatinib vs no imatinib per progression survival
Information on the clinical evidence and effectiveness – main outcome of the study	Sample patients/study sample/ patient groups	46 imatinib group 47 no imatinib (historical) group
	Study design	Retrospective follow up case–control study based on medical records
	Effectiveness analysis	Kaplan–Meier estimates of OS and imatinib and historical groups
	Effectiveness measures and results/outcome measures	
	Primary end points/outcome and secondary end points/ outcome Statistical precision of these outcomes	*Median OS (months)* Imatinib 66.7 No imatinib 7.7 *Median PFS (months)* Imatinib 45.3 No imatinib 5.6 *OS at 1 year* Imatinib 95.4% No imatinib 32.6% *PFS at 1 year* Imatinib 81.4% No imatinib 17.4%
	Clinical recommendations and conclusion	Patient receiving imatinib had significantly longer median OS and median PFS, and higher 1-year OS and 1-year PFS than the historical group

Economic analysis	Measures of health outcome/ benefits used in the economic analysis	OS, PFS and life-year gained
	Direct costs and its components	*Details provided in methods section on actual cost of drugs, labour and supply, but no results given*
	Prospective or retrospective (depend on study design)	Mean costs per patient: $79,829 imatinib; $1743 no imatinib
	Whether values were imputed in for certain cases	Costs of surgery or radiotherapy not included (though similar in both arms)
	How hospital stay was defined, and whether any classifications were used or not	
	Costing of complications or side effects	Did not include the cost of side effects, cost of health-care visits, or supportive care
	Estimations of unit costs and source/methods	Cost of drugs presumably include cost of side effects treatment
	Indirect costs and its components	
	Cost of productivity, cost of volunteer care and support for the patient	Not included
	Currency, year prices	C$, 2006 prices
	Sensitivity analysis	Conducted univariate sensitivity analysis to examine the impact of upper and lower values of the cost of the drugs, the cost of treatment, the utilities of successful treatment and PD, the time horizon, and the annual rate of discount. They used imatinib at a 600 mg/day dose to examine the impact of results variation as an alternative scenario for the sensitivity analysis
Results/major findings	Benefits results from the economic evaluation	Mean OS from imatinib 66.7 months, and historical control group 7.7 months
		Mean PFS – 45.3 months vs 5.6 months
	Costs results used in the economic evaluation	Cost of treatment, costs to health sector (cost to NHS)
		Major determinants of costs, the principle costs drivers
	Synthesis of costs and benefits	Conducted the sensitivity analysis
	Author conclusion/ recommendations	Imatinib cost-effective in treatment of GIST with an ICER of $15,882

BCCA, British Columbia Cancer Agency.

Study identification	Author and year	Paz-Ares 2008[99]
	Intervention studied/ comparators	Sunitinib (50 mg/day) with BSC and BSC alone
	Hypothesis/question	Assess cost-effectiveness of sunitinib vs BSC as second line of treatment
Key features of the study	Type of study	Full economic evaluation (cost-effectiveness analysis)
	Target population/sample population	Hypothetical cohort of Spanish population with GIST after progression with imatinib. Perspective – Spanish national health system
	Context/settings	Patients with advanced unresectable GIST, intolerant to or with diseases progressing during treatment with imatinib
	Dates to which the data of the study relate	Used Demetri *et al.* 2006 study[52]
	Source of effectiveness data	Used Demetri *et al.* 2006 study[52]
		Expert panel, three pathology experts, three health economists
	Modelling	Markov model
	Link between effectiveness and costs data	Data reported by expert panel on number of visits to oncology clinic, laboratory tests, CT scans, nurse visits, visits to palliative units and analgesic drugs. QoL obtained from EQ-5D scores of A6181004 (Demetri study population)

Information on the clinical evidence and effectiveness – main outcome of the study	Sample patients/study sample/ patient groups	Hypothetical cohort of patients with advanced unresectable GIST, intolerant to or with disease progressing during treatment with imatinib (same as Demetri study??)
	Study design	Decision model analysis, based on the trial[52]
	Effectiveness analysis	LYG, QALY
		Progression-free life-years
		Total mean cost per patient
		Cost per QALY gained
		ICER
	Effectiveness measures and results/outcome measures	
	Primary end points/outcome and secondary end points/ outcome	OS, LYG
		PFS
	Statistical precision of these outcomes	Incidence and treatment of adverse effects
	Clinical recommendations and conclusion	According to oncology thresholds for oncology patients, sunitinib is considered better
Economic analysis	Measures of health outcome/ benefits used in the economic analysis	QoL obtained from EQ-5D scores
	Direct costs and its components	*Total mean costs/patient*
		€23,259 in sunitinib group (including costs of adverse events) as against €1622 for BSC
	Indirect costs and its components	
	Cost of productivity, cost of volunteer care and support for the patient	Not included
	Currency, year prices	€, 2007 prices
	Statistical analysis/cost (whether parametric or non-parametric boot strap used to generate the CIs around each difference in costs and differences in total costs	Deterministic
	Sensitivity analysis	Univariate sensitivity analysis

Results/major findings	Benefits results from the economic evaluation	Patients benefits in LYG: 1.59 (for sunitinib + BSC) vs 0.88 (BSC)
		Progression-free life-years: 0.50 (sunitinib) vs 0.24 (BSC)
		QALY 1 vs 0.55
	Costs results used in the economic evaluation	Total mean costs/patients:
		€23,259 vs €1622
	Synthesis of cost and benefits	Treatment with sunitinib vs BSC resulted in patients' benefits of 0.26 progression-free life-years, 0.71 LYG and 0.45 QALYs gained with the cost difference of €21,637/per patient between both treatments
		ICER of sunitinib vs BSC:
		i. per LYG €30,242
		ii. per month of PFS €4090
		iii. per QALY gained €49,090
		Univariate sensitivity analysis
		The most important variables:
		OS HR
		Cost of sunitinib
		Utility value during active treatment and after progression
	Any attempt to consider the uncertainty surrounding estimates of effects	Yes, considered the uncertainty surrounding estimates of effects
		Considering ± 25% variation on the OS, the parameter most influencing the model results, the ICER/QALY gained would oscillate between €39,201 and €62,806
	Author conclusion/ recommendations	Sunitinib can be considered cost-effective vs BSC with acceptable cost per LYG and QALY gained
		Notes the limitation in using an extrapolated survival curve

Study identification	Author and year	Huse 2007[97]
	Intervention studied/ comparators	Imatinib in the treatment of advanced GIST
	Hypothesis/question	Estimated the cost-effectiveness of imatinib mesylate in treatment of unresectable GIST using trials data elsewhere and using them in US context
Key features of the study	Type of study	Cost-effectiveness modelling for decision analysis
	Target population/sample population	Advanced GIST patients
	Context/settings	USA, imatinib mesylate treatment vs no treatment of advanced hypothetical GIST population in USA
	Dates to which the data of the study relates to	Mostly trial data used: Demetri *et al.* 2002[38] trial data and Blanke trial[39,103,117] data and Phase II clinical trial data
	Source of effectiveness data	Demetri *et al.* 2002[38] trial data and Blanke trial[39,103,117] data
	Modelling	Decision modelling
	Link between effectiveness and costs data	Imatinib cost: *Pharmacy's Fundamental Reference*. Montvale, NJ: Thomson Health Care; 2005, and *Physicians' Desk Reference 2005*. Montvale, NJ: Thomson PDR; 2005
		Cost of medical management for pancreatic cancer was used in absence of data for GIST management
		Cost data for diseases specific
		For palliative care – as GIST-specific palliative care data not available, information on palliative care for pancreatic cancer was used

Information on the clinical evidence and effectiveness – main outcome of the study	Sample patients/study sample/ patient groups	Hypothetical cohort population with advanced GIST
	Study design	Decision model
	Effectiveness analysis	QALY
	Effectiveness measures and results/outcome measures	Used from UK study (Wilson *et al.*[55])
	Primary end points/outcome and secondary end points/ outcome	Utilities
		0.875 for PD (lower bound 0.75 to 1.00 upper)
	Statistical precision of these outcomes	0.935 for successful treatment (0.4 to 1.00)
	Clinical recommendations and conclusion	Imatinib is cost-effective in advanced GIST patients
Economic analysis	Measures of health outcome/ benefits used in the economic analysis	QALY, OS, cost, cost per LYG and cost per QALY gained
	Indirect costs and its components	
	Cost of productivity, cost of volunteer care and support for the patient	Not included
	Currency, year prices	US$, 2005 prices
	Sensitivity analysis	One-way sensitivity analysis
Results/major findings	Benefits results from the economic evaluation	Effectiveness QALYs – 4.15 for imatinib, 2.23 for untreated
		Difference (treated – untreated) 1.92
		The net discounted cost of achieving the survival benefit of 2.2 QALY (PV of 1.9 QALY) is US$74,369 per imatinib-treated patient
		CER – US$38,723
	Costs results used in the economic evaluation	Imatinib treatment US$416,255
		Untreated US$341,886
	Cost of treatment, costs to health sector (cost to NHS)	Weekly cost of imatinib: $US685 (685 to 1028)
		Weekly costs of care successfully treated patients: US$359 (226 to 492)
	Major determinants of costs, the principle costs drivers	Weekly cost of care for PD: US$2575 (1700 to 3450)
		Utilities of successful treatment and PD: 0.935, 0.875, respectively
		Time horizon (years): 10, 20 in sensitivity analysis
		Major cost drivers – cost of drugs
	Synthesis of cost and benefits	The cost-effectiveness ratio was most sensitive to variation in the cost estimates and time horizon for the analysis
	Any attempt to consider the uncertainty surrounding estimates of effects	CER ratios were estimated for the upper and lower bound of the parameters
	Author conclusion/ recommendations	Over 10 years' time horizon, imatinib treatment increases mean quality-adjusted survival from 2.4 to 4.6 QALYs, this gain of 2.2 QALYs (undiscounted) with PV of 1.92 QALYs. Net undiscounted cost of achieving this survival benefit is US$74,369 per imatinib-treated patient, yielding a cost-effectiveness ratio of US$38,723 per QALY

PV, present value.

Study identification	Author and year	Teich 2009[100]
	Intervention studied/ comparators	Sunitinib vs imatinib 800 mg/day, and BSC for those who failed with imatinib 400 mg/day
	Hypothesis/question	What is the cost-effectiveness of sunitinib vs imatinib in second-line treatment for GIST in Brazil
Key features of the study	Type of study	Model analysis
	Target population/sample population	Cohort population failed with imatinib 400 mg/day
	Dates to which the data of the study relate	Not specified, 2005 prices used
	Modelling	Markov model
	Link between effectiveness and costs data	Cost per LYGs, cost per progression-free life-years
		ICER
Information on the clinical evidence and effectiveness – main outcome of the study	Sample patients/study sample/ patient groups	Cohort population number 1000
	Study design	Modelling
	Effectiveness analysis	In comparison with BSC sunitinib increases life-years and progression-free life-years by 0.3 and 0.26 years, respectively
		With incremental costs of R$86,756 (US$61,968, PPP 2005)
		In comparison with imatinib, sunitinib was more effective and cost-effective with increased life-year of 0.02 and progression-free LYG of 0.47, and less costly over 6 years
Results/major findings	Author conclusion/ recommendations	Sunitinib is cost-effective when compared with imatinib 800 mg/day and BSC

Study identification	Author and year	Wilson 2005[55]
	Intervention studied/ comparators	Cost-effectiveness of imatinib in the treatment of unresectable and/or metastatic KIT-positive GIST relative to current standard practice
	Hypothesis/question	Assess the clinical effectiveness and cost-effectiveness of imatinib in the treatment of unresectable and/or metastatic KIT-positive GIST relative to current standard practice
Key features of the study	Type of study	Systematic review of clinical effectiveness and economic evaluation
	Target population/sample population	Hypothetical cohort population with unresectable GIST in UK
	Context/settings	UK NHS perspective
	Dates to which the data of the study relates to	2004?
	Source of effectiveness data	Trials
		Novartis model from clinical trial
	Modelling	Markov modelling
		Reporting results from two modelling works
		1. Novartis model
		2. Birmingham model
	Link between effectiveness and costs data	ICER, cost per QALY

Information on the clinical evidence and effectiveness – main outcome of the study	Sample patients/study sample/ patient groups	Trial patients – 147 patients with malignant unresectable and/or metastatic GISTs with median follow-up 25 months
		Modelled for 10 years
	Study design	Open-label multicentre trial compared two imatinib doses: 400 or 600 mg/day
	Effectiveness analysis	The survival rate was 88% after 1 year and 78% after 2 years
	Clinical recommendations and conclusion	The survival rate was 88% after 1 year and 78% after 2 years
Economic analysis	Measures of health outcome/ benefits used in the economic analysis	QALYs from ECOG performance of the trial patients
	Direct costs and its components	
	Prospective or retrospective (depend on study design)	Prospective as trial data
	Whether values were imputed in for certain cases	Values were not imputed as patients' data were used from trials
	How hospital stay was defined, and whether any classifications were used or not	
	Costing of complications or side effects	Costs of side effects were available from patients' data
	Estimations of unit costs and source/methods	*From Novartis model*
		Drug cost of imatinib £20,000
		Costs of outpatient visits £440 per year
		Cost of CT scan £656 for imatinib patients and £82 for patients with PD
		Cost of GP visits £40 per year
		Cost of management of adverse events £159 per year (range £127.20–190.80)
		Costs discounted at 6% (sensitivity – 3% and 6%)
		QALY discounted at 1.5% (sensitivity – 1.5–3%)
		Birmingham model developed for this report
		4 weeks
		Cost of adverse event £12.23
		Cost of imatinib 400 mg £1453.54
		Cost of imatinib 600 mg £1874.49
		Costs of no treatment (BSC) £43.23
		Cost of terminal disease (death) £2730
		Discounted rate for cost 0.0046154
		Discounted rate for QALY 0.0011538
		Other costs for imatinib-treated patients £87.38
		Utility for imatinib 0.935
		Utility for progressive state 0.875
		Using incidence rate used by Novartis (15 per million population) and assuming 10–30% of all GIST patients expected to have metastatic and/or unresectable disease, the number of patients treated with metastatic and/or unresectable disease would be between 80 and 240, and the budgetary impact on the NHS is estimated at between £2.4M and £11.8M per year. The costs to the NHS per patient at £20,400 per year
	Indirect costs and its components	Not included
	Currency, year prices	£, 2004 prices

Results/major findings	Benefits results from the economic evaluation	The cost per QALY ranged from £51,515 to £98,889 after 2 years and from £27,331 to £44,236 after 5 years and from £21,404 to £33,976 after 10 years
		Results from Birmingham model
		ICER changes depending whether Weibull or exponential distribution is used
		Weibull ICER – £26,427
		Exponential ICER £21,707
	Costs results used in the economic evaluation	*From Novartis model*
		Drug cost of imatinib £20,000
	Cost of treatment, costs to health sector (cost to NHS)	Costs of outpatient visits £440 per year
		Cost of CT scan £656 for imatinib patients and £82 for patients with PD
	Major determinants of costs, the principle costs drivers	Cost of GP visits £40 per year
		Cost of management of adverse events £159 per year (range £127.20–190.80)
		Weekly cost of imatinib (pooled trial data) £420.38 (£420.38–370.38; 400 mg per day start dose)
		Other costs per imatinib-treated patients £1136 (£1786–570)
		Others costs per PD patients £562 (£1498–233)
		Utilities:
		Imatinib treated 0.935 (0.900–0.935)
		Progressive 0.875 (0.875)
		Birmingham model developed for this report
		4 weeks
		Cost of adverse event £12.23
		Cost of imatinib 400 mg £1453.54
		Cost of imatinib 600 mg £1874.49
		Costs of no treatment (BSC) £43.23
		Cost of terminal disease (death) £2730
		Discounted rate for cost 0.0046154
		Discounted rate for QALY 0.0011538
		Other costs for imatinib-treated patients £87.38
		Utility for imatinib 0.935
		Utility for progressive state 0.875
	Synthesis of cost and benefits	Yes costs, discount rate, cost for acquisition of drugs
	Any attempt to consider the uncertainty surrounding estimates of effects	
	Author conclusion/ recommendations	The Novartis model suggested that the costs per QALY gained ranged from £51,515 to £98,889 after 2 years, from £27,331 to £44,236 after 5 years and from £21,404 to £33,976 after 10 years. This range of estimates may still not reflect the uncertainty, as the estimates after 2 years are mainly based on mathematical extrapolation beyond observed data. The results from the Birmingham model confirm the findings of the Novartis model
		Because there were no directly controlled trials the results for the model cannot be very conclusive owing to the uncertainties

Study identification	Author and year	Reddy 2007[54]
	Intervention studied/ comparators	NA
	Hypothesis/question	NA
Key features of the study	Type of study	Systematic review to identify, summarise and evaluate published studies and abstracts describing the epidemiological, HRQoL and economic impact of GIST 2000–6 34 publications 29 provided data on epidemiology One provided cost data Three reported HRQoL One reported cost and HRQoL
	Target population/sample population	NA
	Context/settings	NA
Economic analysis	Measures of health outcome/ benefits used in the economic analysis	Performance stated was assessed using ECOG scale performance take from Demetri *et al.* study[52]
Results/major findings	Costs results used in the economic evaluation	The acquisition costs of imatinib were estimated at $18 per 100-mg tablet in the USA and €23 in France
	Cost of treatment, costs to health sector (cost to NHS)	Annual cost $32,850 in the USA and €41,975 in France (assuming 50% of patients each received 400 or 600 mg/day)
	Major determinants of costs, the principle costs drivers	UK study Annual drug cost £20,000 Outpatient visits including laboratory tests £440 GP visits £40 per year CT scans £656 for imatinib patients and £82 for patients with PD Management of adverse events: £159 (range £127–191) Another study (model base Wilson *et al.*[55]) Annual costs of imatinib were £18,896 and £24,368 for patients on 400 and 600 mg daily, respectively
	Synthesis of cost and benefits	Total costs with imatinib over 2 years £30,295 and for 10 years £47,521
	Any attempt to consider the uncertainty surrounding estimates of effects	BSC – £1949 at 2 years and £4047 at 10 years Cost QALY gained £85,224 after 2 years and £29,789 after 10 years Total costs were £31,160 at 2 years compared with £56,146 at 10 years with imatinib vs £1998 and £4230 at 2 and 10 years, respectively, with BSC The cost per QALY gain varied from £45,533 to £70,206 at 2 years and from £21,708 to £25,859 at 10 years

Study identification	Author and year	Hopkins 2008[101]
	Intervention studied/ comparators	Sunitinib and imatinib, and placebo (different studies reviewed)
	Hypothesis/question	Review the new developments in therapeutic cancer drugs
Key features of the study	Type of study	Review
	Target population/sample population	GIST patients, patients with diseases resistant to imatinib 800 mg/day or intolerant of imatinib
		Sample not applicable
	Context/settings	Settings of the clinical trials for sunitinib
		Three trials
		Phase III, 56 sites, Europe, America, Asia and Australia
	Dates to which the data of the study relate	2003, 2004, 2005 and 2009
	Source of effectiveness data	Reviewed from all the studies mentioned
	Modelling	Not applicable
	Link between effectiveness and costs data	Not relevant
Information on the clinical evidence and effectiveness – main outcome of the study	Sample patients/study sample/ patient groups	Maki[118] 2005 – 97
		Demetri 2006[52] – 207 and 105 (placebo)
		George[119] 2007 – 60
	Clinical recommendations and conclusion	Initial results for use of sunitinib are promising; however, too early to draw conclusion
		Important to consider the secondary resistance in GIST
		Mutational status should be determined before treatment in order to decide the initial dosage of kinase inhibitor
Economic analysis	Measures of health outcome/ benefits used in the economic analysis	Referred to SMC study[120]
	Direct costs and its components	
	Prospective or retrospective (depend on study design)	Not relevant – did not use or refer to studies with costing of the intervention
		Refer to SMC study[120]
	Whether values were imputed in for certain cases	Drug costs for one 6-week cycle of sunitinib 50 mg – £3304 for the 4–2 regimen – 4-cycle costing over £1300
	How hospital stay was defined, and whether any classifications were used or not	
	Costing of complications or side effects	
	Estimations of unit costs and source/methods	
	Indirect costs and its components	
	Cost of productivity, cost of volunteer care and support for the patient	Not considered
	Currency, year prices	Drug costs at 2006 prices
	Statistical analysis/cost	
	Sensitivity analysis	

Results/major findings	Benefits results from the economic evaluation	
	Costs results used in the economic evaluation	Drugs costs – UK NHS
	Cost of treatment, costs to health sector (cost to NHS)	The total costs were not reported for the study reviewed. The costs are not from study reviewed
	Major determinants of costs, the principle costs drivers	
	Synthesis of cost and benefits:	There was not a complete economic evaluation either referred or modelled in this study
		So synthesising not relevant
	Any attempt to consider the uncertainty surrounding estimates of effects	No
	Author conclusion/ recommendations	No recommendation from economic evaluation

SMC, Scottish Medicines Consortium.