Technology Assessment Report commissioned by the NETSCC HTA Programme on behalf of the National Institute for Health and Clinical Excellence

HTA 08/226/01

FINAL PROTOCOL

February 2011

1 Title of the project:

Dasatinib, nilotinib and standard dose imatinib for the first-line treatment of chronic myeloid leukaemia (including part-review of TA 70)

2 Name of TAR team and project 'lead'

PenTAG, Peninsula College of Medicine and Dentistry, University of Exeter

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3 Plain English Summary

Chronic myeloid leukaemia is one of the blood cancers. Although it has serious consequences for the patient, the outlook with treatment is more favourable than might be expected. The typical age when chronic myeloid leukaemia becomes apparent is between 50 and 60 years and the average life expectancy is at least 15 years.

This project will examine the evidence on how good a number of drugs (dasatinib, nilotinib and standard dose imatinib) are for treating chronic myeloid leukaemia immediately after the disease has been diagnosed, as the first treatment that the patient receives. Concerning this use, the project will update the evidence previously presented to the National Institute of Health and Clinical Excellence in the case of imatinib and review for the first time evidence on dasatinib and nilotinib. The assessment will also assess whether the reviewed drugs are likely to be considered good value for money for the NHS.

4 Decision problem

4.1 Purpose

Chronic myeloid leukaemia (CML) is one of the blood cancers in which there is an overproduction of one type of white blood cell, the granulocytes, by the bone marrow. CML progresses slowly through three identifiable phases: the chronic phase, the accelerated phase and the blast crisis (transformation) phase, with the latter two being grouped together as advanced phase. In some cases categorisation can be difficult and there are various criteria for defining the three phases of CML.

The majority of people are diagnosed in the chronic phase. The course of the chronic phase is initially stable with most people remaining responsive to treatment; around 60% of people will remain in chronic phase and in complete cytogenic remission for at least 5 years. From the chronic phase, people with CML either go through the accelerated phase or move straight into blast crisis. The accelerated phase is a poorly defined period. Blast crisis generally lasts for between 3-6 months and is a terminal stage in which the disease transforms into a fatal acute leukaemia.

Ninety-five percent of people with CML have a specific chromosomal abnormality commonly known as the 'Philadelphia chromosome'. This is caused by an exchange of genetic material between two chromosomes (known as reciprocal translocation); between parts of the long arms of chromosome 22 and chromosome 9. It is associated with fusion of the breakpoint cluster region (BCR) and Abelson (ABL) genes and the production of an abnormal tyrosine kinase oncoprotein. BCR-ABL is the only known cause of CML.

CML is a rare disease with an incidence of approximately 1 per 100,000 people every year. It accounts for about one in six cases of leukaemia in adults. Approximately 600 to 800 people are diagnosed with CML in England and Wales each year. It has been estimated that median life expectancy is at least 15 years. The median age at diagnosis is between 50 and 60 years.

NICE technology appraisal guidance 70 in 2003 [1] [2] recommends imatinib, a tyrosine-kinase inhibitor, as first-line treatment for people with Philadelphia chromosome positive CML in the chronic phase. However since then other tyrosine-kinase inhibitors have been developed and are being used in the initial treatment of CML. NICE is thus up-dating TAG 70 concerning the evidence on imatinib, and considering for the first time evidence on dasatinib and nilotinib as first-line treatment for people with Philadelphia chromosome positive CML in the chronic phase. The question

referred to NICE is, “To appraise the clinical and cost effectiveness of dasatinib, nilotinib and standard-dose imatinib within their licensed indications for the first-line treatment of chronic myeloid leukaemia (including part-review of TA70).”

In addition, outside this appraisal, NICE is currently appraising dasatinib and nilotinib for imatinib-intolerant CML. An appraisal of dasatinib, nilotinib and high-dose imatinib for imatinib-resistant CML (part-review of TA70) is also underway.

4.2 Interventions

The technology assessment report (TAR) will consider three pharmaceutical interventions:

- Dasatinib (Sprycel, Bristol Myers Squibb)
- Nilotinib (Tasigna, Novartis Pharmaceuticals)
- Imatinib (standard dose) (Glivec, Novartis Pharmaceuticals)

All of these are oral tyrosine kinase inhibitors (TKIs). These particular TKIs work by blocking specific signals in cells expressing the BCR-ABL protein, which reduces the uncontrolled proliferation of white blood cells. Imatinib and nilotinib have a high specificity for the BCR-ABL protein, whilst dasatinib acts on multiple targets.

Dasatinib (100mg daily) has a marketing authorisation for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive CML in the chronic phase.

Nilotinib (400/300mg twice daily) has a marketing authorisation for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive CML in the chronic phase.

Imatinib has a marketing authorisation for use in adult and paediatric patients with newly diagnosed Philadelphia chromosome positive CML for whom bone marrow transplantation is not considered as the first-line of treatment. The recommended starting dosage of imatinib is 400mg/day for patients in chronic phase CML. This is the “standard dose” for the purposes of this appraisal.

4.3 Relevant comparators

The main comparators of interest are the alternative interventions particularly:

- Dasatinib vs imatinib (standard dose)
- Nilotinib vs imatinib (standard dose
- Dasatinib vs nilotinib

4.4 Population and relevant sub-groups

Adults with newly diagnosed, chronic phase, Philadelphia chromosome positive CML. If possible newly diagnosed, chronic phase CML without genetic mutation will also be considered, clearly noting that this population is outside the marketing authorisation of the drugs of interest. No other sub-groups of interest have been identified.

4.5 Outcomes to be addressed

The following outcomes will be measured:

- Event-free survival
- Progression-free survival
- Time to progression
- Overall survival
- Response rates – cytogenetic, molecular and haematological
- Time to treatment failure
- Adverse effects of treatment
- Health-related quality of life

5 Methods for synthesis of evidence of clinical effectiveness

The assessment report will include a systematic review of the evidence for clinical effectiveness of dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia. The review will be undertaken following the general principles published by the NHS Centre for Reviews and Dissemination.[3] The components of the review question will be:

Population: Adults with chronic phase CML, naïve to any treatment specifically directed against CML

Interventions: Dasatinib or nilotinib or imatinib (standard dose). Each should be employed in accordance with the marketing authorisation and in the populations indicated in the previous paragraph, noting that CML without genetic mutation is outside the existing marketing authorisations.

Comparators: The alternative interventions, particularly imatinib (standard dose) or nilotinib where the intervention is dasatinib, or imatinib (standard dose) or dasatinib where the intervention is nilotinib.

Outcomes: All potentially relevant outcomes in the included studies will be considered, particularly those capturing:

- Event-free survival
- Progression-free survival
- Time to progression
- Overall survival
- Response rates – cytogenetic, molecular and haematological
- Time to treatment failure
- Adverse effects of treatment
- Health-related quality of life.

Search strategy

The search strategy will comprise the following main elements:

- Searching of electronic databases
- Contact with experts in the field
- Scrutiny of bibliographies of retrieved papers and manufacturer submissions
- Follow-up on mentions of potentially relevant on-going trials noted in previous NICE guidance on imatinib for CML.

The main electronic databases of interest will be:

MEDLINE (Ovid); PubMed; EMBASE; The Cochrane Library including the Cochrane Systematic Reviews Database, Cochrane Controlled Trials Register, DARE, NHS EED and HTA databases; NRR (National Research Register); Web of Science Proceedings; Current Controlled Trials; Clinical Trials.gov; FDA website; EMEA website. These will be searched from search end-date of the last technology appraisal report [2] on this topic October 2002.

The searches will be developed and implemented by a trained information specialist using the search strategy detailed in the technology appraisal by Thomson Coon *et al* as the starting point (see Appendix A for more information).[4]

Inclusion criteria

For the review of clinical effectiveness, in the first instance, only systematic reviews of randomised controlled trials (RCTs) and RCTs will be considered. However, if key outcomes of interest are not measured at all in the included RCTs we will discuss

whether extending the range of included study designs ie to controlled clinical trials could be of value and feasible in the time available with NICE. The systematic reviews will be used as a source for finding further included studies and to compare with our systematic review. Systematic reviews provided as part of manufacturer's submissions will be treated in a similar manner. These criteria may be relaxed for consideration of adverse events, for which observational studies may be included.

Titles and abstracts will be examined for inclusion by two reviewers independently. Disagreement will be resolved by consensus.

Exclusion criteria

Studies will be excluded if they do not match the inclusion criteria, particularly:

- Non-randomised studies (except if agreed, in the absence of RCTs)
- Animal models
- Preclinical and biological studies
- Narrative reviews, editorials, opinions
- Non-English language papers
- Reports published as meeting abstracts only, where insufficient methodological details are reported to allow critical appraisal of study quality.

Data extraction strategy

Data will be extracted independently by one reviewer using a standardised data extraction form and checked by another. Discrepancies will be resolved by discussion, with involvement of a third reviewer if necessary.

Quality assessment strategy

Consideration of study quality will be based on the guidelines set out by the NHS Centre for Reviews and Dissemination [3] and include the following factors for RCTs:

- Timing, duration and location of the study
- Method of randomisation
- Allocation concealment
- Blinding
- Numbers of participants randomized, excluded and lost to follow up.
- Whether intent to treat analysis is performed

- Methods for handling missing data
- Appropriateness of statistical analysis.

This framework will be adapted should other study designs subsequently be included. Quality will be assessed independently by one reviewer and checked by another, discrepancies again being resolved by discussion, with involvement of a third reviewer if necessary.

Methods of analysis/synthesis

Data will be tabulated and discussed in a narrative review. Where appropriate, meta-analysis will be employed to estimate a summary measure of effect on relevant outcomes based on intention to treat analyses.

Meta-analysis will be carried out using fixed and random effects models, using RevMAN supplemented with STATA or equivalent software as required. Heterogeneity will be explored through consideration of the study populations, methods and interventions, by visualisation of results and, in statistical terms, by the χ^2 test for homogeneity and the I^2 statistic. Mixed treatment comparisons will be used as far as data allows to facilitate comparison between the drugs for which there is no direct comparison.

6 Methods for synthesising evidence of cost-effectiveness

6.1 Review question

For the interventions and populations indicated above, the existing evidence on cost-effectiveness will be systematically reviewed.

6.2 Search strategy

The searches will again be developed and implemented by a trained information specialist using the search strategy detailed in the technology appraisal by Thomson Coon *et al* [4] as the starting point. The range of sources searched will include those for clinical effectiveness and extend to include NHS EED and Econlit. October 2002 will again be the starting point.

6.3 Study selection criteria and procedures

The inclusion and exclusion criteria for the systematic review of economic evaluations will be identical to those for the systematic review of clinical effectiveness, except:

Non-randomised studies will be included (e.g. decision model based analyses, or analyses of patient-level cost and effectiveness data alongside observational studies).

Full cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses and cost consequence analyses will be included. (Economic evaluations which only report average cost-effectiveness ratios will only be included if the incremental ratios can be easily calculated from the published data.)

Stand alone cost analyses based in the UK NHS will also be sought and appraised.

Based on the above inclusion/exclusion criteria, study selection will be made by one reviewer. In addition, a random sample of the inclusion decisions will be checked by a second reviewer.

6.4 Study quality assessment

The methodological quality of the economic evaluations will be assessed by one reviewer according to internationally accepted criteria such as the Consensus on Health Economic Checklist (CHEC) questions developed by Evers *et al*.[5] Any studies based on decision models will also be assessed against the International Society for Pharmacoecnomics and Outcomes Research (ISPOR) guidelines for good practice in decision analytic modelling.[6]

6.5 Data extraction strategy

Data will be extracted by one researcher into two summary tables: one to describe the study design and characteristics of each economic evaluation and the other to describe the main results. The tables may need to be split into a number of sub-tables if the number of included studies is large. The entries will be checked by a second reviewer.

In the study design table the main headings will include: author and year; model type or trial based; study design (e.g. cost-effectiveness analysis [CEA], cost utility analysis [CUA] or cost-analysis); service setting/country; study population; comparators; research question; perspective, time horizon, and discounting; main costs included; main outcomes included; sensitivity analyses conducted; and other notable design features.

For modelling-based economic evaluations a supplementary Study Design table will record further descriptions of: model structure (and note its consistency with the study perspective, and knowledge of disease/treatment processes; sources of

transition and chance node probabilities; sources of utility values; sources of resource use and unit costs; handling of heterogeneity in populations; evidence of validation (e.g. debugging, calibration against external data, comparison with other models).

In the results table for each comparator we will show; incremental cost; incremental effectiveness/utility and incremental cost-effectiveness ratio(s). Excluded comparators on the basis of dominance or extended dominance will also be noted. The original authors' conclusions will be noted, and also any issues they raise concerning the generalisability of results. Finally the reviewers' comments on study quality and generalisability (in relation to the TAR scope) of their results will be recorded.

6.6 Synthesis of extracted evidence

Narrative synthesis, supported by the data extraction tables, will be used to summarise the evidence base.

7 Economic Modelling

The general approach will be consistent with the NICE reference standard.[7] A new cost-effectiveness analysis will be carried out from the perspective of the UK NHS and Personal Social Services (PSS) using a decision analytic model. This will build on the modelling approach used in a recent technology appraisal by PenTAG on a closely related topic [4] and be informed by modelling approaches used in other related NICE appraisals and published cost-effectiveness literature reviewed (see Section 6).

Model structure will be determined on the basis of available research evidence and clinical expert opinion.

The sources of parameter values that determine the effectiveness of the interventions being compared will be obtained from our own systematic review of clinical effectiveness or other relevant research literature. Where required parameters are not available from good quality published studies in the relevant patient group we may use data from manufacturer submissions to NICE.

Cost data will be identified from NHS and PSS reference costs or, where these are not relevant, will be extracted from published work and/or sponsor submissions to NICE. If insufficient data are retrieved from published sources, costs may be derived from individual NHS Trusts or groups of Trusts.

To reflect health related quality of life, utility values will be sought either directly from relevant research literature or indirectly from quality of life studies.

Analysis of uncertainty will focus on costs and utilities, assuming cost per QALY can be estimated. Uncertainty will be explored through one way sensitivity analysis and, if the data and modelling approach permit, probabilistic sensitivity analysis (PSA). The outputs of PSA will be presented using plots on the cost-effectiveness plane and cost-effectiveness acceptability curves.

A life-time time horizon will be taken for our analysis and both cost and outcomes (QALYs) will be discounted at 3.5%.[7]

We will collate the available relevant material necessary to inform an assessment of the applicability of the End of Life Criteria.

The TAR team cannot guarantee to consider any data or information relating to the technologies if received after 03/06/11.

8 Handling the company submissions

All data submitted by the manufacturers will be considered if received by the TAR team no later than 03/06/11. Data arriving after this date will not be considered.

If the data meet the inclusion criteria for the review they will be extracted and quality assessed in accordance with the procedures outlined in this protocol. Any economic evaluations included in the company submission will be assessed against NICE's guidance on the Methods of Technology Appraisal [7] and will also be assessed for clinical validity, reasonableness of assumptions and appropriateness of the data used. Where the TAR team have undertaken further analyses, using models submitted by manufacturers or via de novo modelling and cost effectiveness analysis, a comparison will be made of the alternative models used for the analysis.

Any 'commercial in confidence' data taken from a company submission will be underlined and highlighted in the assessment

9 Expertise in this TAR team

Name	Institution	Expertise
Toby Pavey	PenTAG, Peninsula Medical School, University of Exeter	Systematic reviewing, project management and overall lead for clinical effectiveness)

Louise Crathorne	PenTAG, Peninsula Medical School, University of Exeter	Systematic reviewing
Tracey Jones-Hughes	PenTAG, Peninsula Medical School, University of Exeter	Systematic reviewing
Martin Hoyle	PenTAG, Peninsula Medical School, University of Exeter	Economic modelling and overall lead for cost-effectiveness
Kevin Marsh	Matrix Knowledge	Health economics (provisional, to be confirmed)
Chris Cooper	PenTAG, Peninsula Medical School, University of Exeter	Information science
Claudius Rudin	Royal Devon and Exeter Foundation Trust	Clinical expert
Ruth Garside	PenTAG, Peninsula Medical School, University of Exeter	Support for systematic reviews
Rob Anderson	PenTAG, Peninsula Medical School, University of Exeter	Overall project lead and project guarantor
Chris Hyde	PenTAG, Peninsula Medical School, University of Exeter	Protocol development

TAR Centre

About PenTAG:

The Peninsula Technology Assessment Group (PenTAG) is part of the Institute of Health Service Research (IHSR) at the Peninsula Medical School. PenTAG was established in 2000 and carries out independent Health Technology Assessments HTAs) for the UK HTA Programme, systematic reviews and economic analyses for the NICE (Technology Appraisal and Centre for Public Health Excellence) and systematic reviews as part of the Cochrane Collaboration Heart Group, as well as for other local and national decision-makers. The group is multi-disciplinary and draws on individuals' backgrounds in public health, health services research, computing and decision analysis, systematic reviewing, statistics and health economics. The Peninsula Medical School is a school within the Universities of Plymouth and Exeter. The IHSR is made up of discrete but methodologically related research groups, among which HTA is a strong and recurring theme.

Recent projects include:

- The effectiveness and cost-effectiveness of donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of TA111): a systematic review and economic model
- Dasatinib and nilotinib for imatinib-resistant or -intolerant chronic myeloid leukaemia: a systematic review and economic evaluation.
- Systematic review of the effectiveness and cost-effectiveness of weight management schemes for the under fives.
- Barriers to and facilitators for the effectiveness of multiple risk factor programmes aimed at reducing cardiovascular disease within a given population: a systematic review of qualitative research.
- Population and community programmes addressing multiple risk factors to prevent cardiovascular disease: a qualitative study into how and why some programmes are more successful than others.
- Barriers to and facilitators of conveying information to prevent first occurrence of skin cancer: a systematic review of qualitative research.
- The harmful health effects of recreational ecstasy: a systematic review of observational evidence.
- The use of surrogate outcomes in model-based cost-effectiveness analyses: a survey of UK health technology assessment reports.
- The effectiveness and cost-effectiveness of cochlear implants for severe to profound deafness in children and adults: a systematic review and economic model.
- The effectiveness and cost-effectiveness of methods of storing donated kidneys from deceased donors: a systematic review and economic model.
- Bevacizumab, sorafenib tosylate, sunitinib and temsirolimus for renal cell carcinoma: a systematic review and economic model.
- The effectiveness and cost-effectiveness of cinacalcet for secondary hyperparathyroidism in end stage renal disease patients on dialysis. systematic review and economic evaluation.

- The effectiveness and cost-effectiveness of carmustine implants and temozolomide for the treatment of newly-diagnosed high grade glioma. Systematic review and economic evaluation.
- The effectiveness and cost-effectiveness of cardiac resynchronisation therapy for heart failure. Systematic review and economic evaluation.
- Inhaled corticosteroids and long-acting beta2-agonists for the treatment of chronic asthma in adults and children aged 12 years and over: a systematic review and economic analysis.
- Inhaled corticosteroids and long-acting beta2-agonists for the treatment of chronic asthma in children under the age of 12 years: a systematic review and economic analysis.
- The cost-effectiveness of testing for hepatitis C (HCV) in former injecting drug users. Systematic review and economic evaluation.

10 Competing interests of authors

None

11 Timetable/milestones

Event	Expected due date
Final scope	04/02/11
Final protocol due	11/02/11
Consultee information meeting (CIM) (if applicable)	To be confirmed
Manufacturers' submissions	03/06/11
ERG Appraisal Report due	06/09/11
1st Appraisal Committee meeting	08/11/11
2nd Appraisal Committee meeting	08/02/12

12 Appendix A

As previously discussed the searches will be developed and implemented by a trained information specialist using the search strategy detailed in the technology appraisal by Thompson Coon *et al* as the starting point.[4]

Chronic Myeloid Leukaemia HTA

Final Search Strategies Jan 2009

Project Manager: Jo Thompson-Coon

Research Fellow: Gabriel Rogers

Modeler: Martin Hoyle

IS: Tiffany Moxham

RE-Run date: 080609

Ovid MEDLINE(R) 1950 to November Week 3 2008

Search Date: 08/01/2009

1 myeloid$ leuk?emia$.mp. 22684

2 myelogenous$ leuk?emia$.mp. 11189

3 myelocytic$ leuk?emia$.mp. 2344

4 exp leukemia, myelogenous, chronic, bcr-abl positive/ or leukemia, myeloid, chronic-phase/ or exp leukemia, myeloid, chronic, atypical, bcr-abl negative/ or exp leukemia, myelomonocytic, chronic/ 12440

5 Leukemia, Myeloid/ 21451

6 5 21451

7 limit 6 to yr="1974 - 1988" 7523

8 Philadelphia Chromosome/ 1797

9 (Philadelphia adj Chromosome).mp. 3699

10 3 or 2 or 4 or 7 or 1 or 8 or 9 44230

11 nilotinib.mp. 141

12 "4-methyl-N-(3-(4-methylimidazol-1-yl)-5-(trifluoromethyl)phenyl)-3-((4-pyridin-3-ylpyrimidin-2-yl)amino)benzamide".mp. [mp=title, original title, abstract, name of substance word, subject heading word] 122

13 tasigna.mp. 7

14 ((amn107 or amn-107 or amn) adj "107").mp. 4

15 14 or 13 or 11 or 12 186

16 dasatinib.mp. 291

17 sprycel.mp. 15

18 (BMS354825 or BMS 354825 or BMS-354825).mp. 57

19 16 or 17 or 18 298

20 10 and 15 137

21 10 and 19 226

22 21 or 20 272

23 (animals not human).sh. 4410095

24 22 not 23 202

25 limit 24 to english language 187

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations January 8, 2009

1 myeloid$ leuk?emia$.mp. 1935

2 myelogenous leuk?emia$.mp. 566

3 myelocytic$ leuk?emia$.mp. 55

4 (Philadelphia adj Chromosome).mp. 151

5 1 or 2 or 3 or 4 2546

6 nilotinib.mp. 83

7 "4-methyl-N-(3-(4-methylimidazol-1-yl)-5-(trifluoromethyl)phenyl)-3-((4-pyridin-3-ylpyrimidin-2-yl)amino)benzamide".mp. 0

8 tasigna.mp. 5

9 ((amn107 or amn-107 or amn) adj "107").mp. 1

10 6 or 7 or 8 or 9 83

11 dasatinib.mp. 139

12 sprycel.mp. 11

13 (BMS354825 or BMS 354825 or BMS-354825).mp. 15

14 11 or 12 or 13 144

15 10 or 14 176

16 5 and 15 123

17 limit 16 to english language 117

EMBASE 1980 to 2009 Week 01

Search Date: 08/01/2009

1 myeloid$ leuk?emia$.mp. 31757

2 myelogenous$ leuk?emia$.mp. 9259

3 myelocytic$ leuk?emia$.mp. 1473

4 chronic myeloid leukemia/ or myeloid leukemia/ 19599

5 Philadelphia 1 Chromosome/ 3678

6 1 or 2 or 3 or 4 or 5 37643

7 nilotinib.mp. 629

8 tasigna.mp. 119

9 (amn107 or amn-107 or (amn adj "107")).mp. 301

10 9 or 8 or 7 641

11 dasatinib.mp. 1016

12 sprycel.mp. 245

13 (BMS354825 or BMS 354825 or BMS-354825).mp. 357

14 11 or 12 or 13 1024

15 ((animal$ or nonhumans) not human$).sh,hw. 1985421

16 10 or 14 1193

17 6 and 16 767

18 17 not 15 754

19 limit 18 to english language 671

Web of Science

Conference Proceedings Citation Index- Science (CPCI-S)--1990-present

Science Citation Index Expanded (SCI-EXPANDED)--1900-present

Via ISI Web of Knowledge online

Search Date: 14 January 2009

9 437 #8 AND Language=(English)

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8 448 #7 AND #4

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

7 733 #6 OR #5

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

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5 317 TS=(nilotinib) OR TS=(tasigna) OR TS=(amn107) OR TS=(amn-107) OR TS=(amn adj "107")

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4 54,363 #3 OR #2 OR #1

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3 2,771 TS=(myelocytic* leukaemia*) OR TS=(myelocytic* leukemia*)

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

2 43,276 TS=(myeloid* leukaemia*) OR TS=(myeloid* leukemia*)

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

1 20,888 TS=(myelogenous* leukemia*) or TS=(myelogenous* leukaemia*)

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

9 **437** #8 AND Language=(English)

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

8 448 #7 AND #4

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

7 733 #6 OR #5

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4 54,363 #3 OR #2 OR #1

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3 2,771 TS=(myelocytic* leukaemia*) OR TS=(myelocytic* leukemia*)

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

2 43,276 TS=(myeloid* leukaemia*) OR TS=(myeloid* leukemia*)

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

1 20,888 TS=(myelogenous* leukemia*) or TS=(myelogenous* leukaemia*)

Databases=SCI-EXPANDED, CPCI-S Timespan=All Years

DARE, NHSEED, HTA via CRD Databases online

Search Date: 14 January 2009

Re-run: 080509: 0 extra

Search Matching records

1 myelogenous* AND leukemia* 17

2 myelogenous* AND leukaemia* 12

3 myeloid* AND leukemia* 38

4 myeloid* AND leukaemia* 44

5 myelocytic* AND leukemia* 0

6 myelocytic* AND leukaemia* 2

7 nilotinib 1

8 tasigna 0

9 amn107 0

10 amn-107 1

11 dasatinib 1

12 sprycel 0

13 BMS354825 0

14 BMS AND 354825 1

15 BMS-354825 1

16 BMS-354825 1

17 BMS-354825 1

18 #1 or #2 or #3 or #4 or #5 or #6 83

19 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 2

20 #18 AND #19 2

UTILITIES SEARCHES April 17, 2009

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1950 to Present

1 myeloid$ leuk?emia$.mp.
23694

2 myelogenous leuk?emia$.mp.
11464

3 myelocytic$ leuk?emia$.mp.
2341

4	(Philadelphia adj Chromosome).mp. 3776	
5	1 or 2 or 3 or 4 37636	
6	nilotinib.mp.	199
7	"4-methyl-N-(3-(4-methylimidazol-1-yl)-5-(trifluoromethyl)phenyl)-3-((4-pyridin-3-ylpyrimidin-2-yl)amino)benzamide".mp.	141
8	tasigna.mp.	8
9	((amn107 or amn-107 or amn) adj "107").mp.	6
10	6 or 7 or 8 or 9	249
11	dasatinib.mp.	434
12	sprycel.mp.	21
13	(BMS354825 or BMS 354825 or BMS-354825).mp.	71
14	11 or 12 or 13	444
15	10 or 14	538
16	5 and 15	338
17	(animals not human).sh. 4356049	
18	16 not 17	261
19	limit 18 to english language	244
20	"Quality of Life"/ 73701	
21	"Value of Life"/ 5023	
22	(life adj2 qualit$3).tw. 87933	
23	quality-adjusted life years/ 3780	
24	(disabilit$3 adj2 life).tw. 1010	
25	daly.tw.	423

26 Health Status Indicators/
13813

27 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirstysix or shortform thirty six or short form thirty six or short form thirtysix or short form thirty six).tw.
9296

28 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
921

29 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve of sftwelve or shortform twelve or short form twelve).tw.
1311

30 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. 16

31 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty of sftwenty or shortform twenty of short form twenty).tw. 284

32 (euroqol or euro qol or eq5d or eq 5d).tw.
1671

33 (euroqol or euro qol or eq5d or eq 5d).tw.
1671

34 (hye or hyes).tw. 48

35 health$ year$ equivalent$.tw. 34

36 health utilit$.ab. 578

37 hui$1.tw. 738

38 disutil$.tw. 114

39 rosser.tw. 65

40 quality of well being.tw. 236

41 quality of wellbeing.tw. 2

42 qwb.tw. 131

43 willingness to pay.tw.
1180

44 standard gamble$.tw. 536

45 (time trade off or time tradeoff).tw. 628

46 (health adj3 (utilit$3 or value$2 or preference$2)).tw.
4391

47 (visual analog$3 scale or VAS).tw.
24685

48 (health adj2 (utilit$3 or value$2 or preference$2)).tw.
2804

49 patient preference$2.tw.
2949

50 or/20-49
166395

51 50 and 5 249

52 51 not 17 243

53 limit 52 to (english language and yr="1990 -Current") 196

54 from 53 keep 1-196 196

55 exp Economics/
400716

56 exp "Costs and Cost Analysis"/
140550

57 exp Cost-Benefit Analysis/
45031

58 "Value of Life"/
5023

59 exp Models, Economic/
6398

60 exp "Fees and Charges"/
23936

61 exp Budgets/
10067

62 (economic$ or price$ or pricing or financ$ or fee$ or pharmacoeconomic$ or pharma economic$).tw.
407483

63 (cost$ or costly or costing$ or costed).tw.
239491

64 (cost$ adj2 (benefit$ or utilit$ or minim$ or effective$)).tw.
61728

65	(expenditure$ not energy).tw. 12993	
66	(value adj2 (money or monetary)).tw.	788
67	(economic adj2 burden).tw. 2142	
68	"resource use".ti,ab. 2726	
69	or/55-68 884540	
70	or/1-3 36277	
71	69 and 70	595
72	71 not 17	524
73	limit 72 to english language	479

NHSEED, via CRD Databases online

Search Date: 17 April 2009

1 myelogenous* AND leukemia* 17

2 myelogenous* AND leukaemia* 12

3 myeloid* AND leukemia* 38

4 myeloid* AND leukaemia* 44

5 myelocytic* AND leukemia* 0

6 myelocytic* AND leukaemia* 2

#7 #1 or #2 or #3 or #4 or #5 or #6

Econlit via First Search

Search Date: 17 April 2009

Myeloid leukaemia

myeloid leukemia

myelogenous leukaemia 0

myelogenous leukaemia 0

myelocytic leukaemia

myelocytic leukemia

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