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27 May 11

Dear Sir/Madam,

SPIRIT 2 - A phase III, prospective randomised comparison of imatinib (STI571, Glivec/Gleevec) 400mg daily versus dasatinib (Sprycel) 100mg daily in patients with newly-diagnosed chronic phase chronic myeloid leukaemia.

EUDRACT number: 2007-006185-15
REC Reference: 07/H0718/90

Please find enclosed the Annual Safety Report for the above study.

If you have any queries regarding the report please don't hesitate to contact the Chief Investigator (Prof. S G O'Brien) or myself.

Yours sincerely,

A handwritten signature in blue ink that reads "C. Hedgley".

Corinne Hedgley
Senior Trial Project Manager.

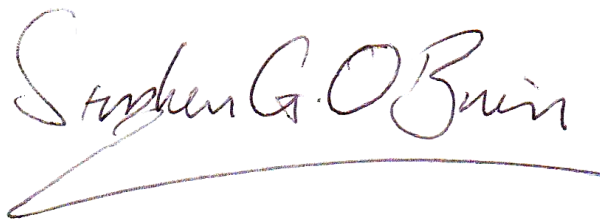
cc Amanda Tortice
R&D Manager, Newcastle-upon-Tyne Hospitals NHS Foundation Trust

Annual Safety Report

Study Title	SPIRIT 2 - A phase III, prospective randomised comparison of imatinib (STI571, Glivec/Gleevec) 400mg daily versus dasatinib (Sprycel) 100mg daily in patients with newly-diagnosed chronic phase chronic myeloid leukaemia.
EUDRACT Number	2007-006185-15
ISRCTN Number	ISRCTN54923521
MREC Reference	07/H0718/90
Chief Investigator	Prof. S. G. O'Brien
SPONSOR	Newcastle upon Tyne Hospitals NHS Foundation Trust
Reporting Period	April 2010 – April 2011

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27 May 2011

Prof. S. G. O'Brien (Chief Investigator)

Date

1 Report on the subjects' safety

Study enrolment began in August 2008. Between August 2008 and April 2010, 202 patients were randomised as follows;
101 patients on 400mg imatinib daily
101 patients on 100mg dasatinib daily
Recruitment is ongoing.

For the reporting period (April 2010 to April 2011) there were no SUSARs and 32 SARs reported to the sponsor.

There have been no major safety issues to report with the trial.

The incidence of SAE/SAR's continues to be higher in the Dasatinib arm. We are continuing to monitor this carefully but believe it is probably partly due a cautious approach by study sites in handling adverse events due to the relative inexperience with this drug in comparison to imatinib.

There have been 29 reports of pleural effusion (in 24 patients) on the dasatinib arm (11% of patients) (none on the imatinib arm). Ten of these have required a chest drain and 7 have lead to study treatment discontinuation. The study team are actively monitoring reports of suspected plural effusions. The Dasatinib SmPC lists pleural effusions as 'very common' seen in 18% of patients.

The safety data were reviewed by the study DMC on the 20th April 2011. The DMC advised that they were happy for the trial to continue.

2 Line listing of all suspected SARs (including all SUSARs)

IDENTIFIERS				SAE DETAILS			CAUSALITY	STUDY DRUG DETAILS					
Patient Number	CASE ID	AGE (yrs)	SEX	ONSET DATE	DIAGNOSIS	OUTCOME	IMATINIB/DASATINIB	DRUG NAME	DOSE/UNITS/FREQUENCY/ ROUTE				DRUG START
0024	N0000353.0024.01	81	M	20MAY09	CHEST PAIN	RECOVERED WITH SEQUELAE	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	8MAY09
0043	N0000291.0043.01	58	F	24JUN09	LEFT LOWER ZONE CONSOLIDATION LUNG.	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	19JUN09
0057	N0000194.0057.03	73	F	30AUG09	DIARRHOEA	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	18AUG09
0019	N0000046.0019.01	58	F	17JUN09	GRADE 3/4 SKIN REACTION COVERING >50% OF BODY	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	28APR09
0043	N0000291.0043.02	58	F	6SEP09	DIARRHOEA + PYREXIA	COMPLETELY RECOVERED	DASATINIB	DASATINIB	80	MG	DAILY	ORAL	27AUG09
0078	N0000111.0078.01	48	M	10SEP09	SHORT OF BREATH ON EXERTION POSSIBLY SECONDARY TO ATRIAL FIBRILLATION	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	1SEP09
0042	N0000157.0042.01	45	M	14OCT09	GRADE 4 ANAEMIA	CONDITION IMPROVING	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	4SEP09
0057	N0000194.0057.05	73	F	14OCT09	CONGESTIVE CARDIAC FAILURE SECONDARY TO DIASTOLIC DYSFUNCTION	CONDITION IMPROVING	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	8AUG09
0043	N0000291.0043.04	58	F	21DEC09	PROFUSE DIARRHOEA, ABDO DISCOMFORT - ? DEHYDRATED	COMPLETELY RECOVERED	DASATINIB	DASATINIB	50	MG	DAILY	ORAL	24NOV09
0013	N0000239.0013.01	58	F	--DEC09	LEFT VENTRICULAR FAILURE	CONDITION IMPROVING	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	3MAR09
0138	N0000326.0138.01	64	M	--MAR10	LARGE (7.7CM X 6.0CM) RENAL MASS	CONDITION STILL PRESENT AND UNCHANGED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	5JAN10
0007	N0000046.0007.01	72	F	3MAR10	PLEURAL EFFUSION	CONDITION STILL PRESENT AND UNCHANGED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	5JAN10
0011	N0000072.0011.01	68	M	8APR10	POSSIBLE BRONCHIAL CARCINOMA	CONDITION STILL PRESENT AND UNCHANGED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	27JAN09
0171	N0000028.0171.01	53	M	13APR10	NEUTROPENIC SEPSIS ? RELATD TO DENTAL CARIES	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	8MAR10
0027	N0000666.0027.01	45	F	07SEP09	DEVELOPMENT OF EMPHYSEMA RESULTING IN DYSPNOEA ON EXERTION	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	18MAY09
0191	N0000239.0191.01	68	F	13MAY10	ANAEMIA AND THROMBOCYTOPENIA	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	15APR10

0192	N0000072.0192.01	30	M	20MAY10	ACUTE ONSET RIGHT HIP PAIN	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	08APR10
0171	N0000028.0171.02	53	M	18MAY10	NEUTROPENIA	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	18MAY09
0228	N0000267.0228.01	64	M	21JUN10	ACUTE PANCREATITIS	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	16JUN10
0212	N0000008.0212.02	67	F	27JUN10	WORSENING HEART FAILURE	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	22MAY10
0254	N0000050.0254.01	34	M	24JUL10	RASH AND FEVER UNKNOWN CAUSE	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	14JUL10
0243	N0000132.0243.01	79	F	19JUL10	FEVER, PULMONARY OEDEMA	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	22JUN10
0134	N0000339.0134.01	66	F	02AUG10	ENLARGED HEART, BILATERAL PLEURAL EFFUSIONS	CONDITION STILL PRESENT AND UNCHANGED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	21DEC09
0239	N0000102.0239.01	48	F	05AUG10	NAUSEA/ DIARRHOEA FOLLOWING IMATINIB HEADACHE/ NEURALGIA, SEVERE TIREDNESS	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	29JUN10
0083	N0000105.0083.01	74	M	UKJUL10	KERATOACRTHOMA	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	15SEP09
0198	N0000039.0198.02	53	M	26MAY10	STABLE ANGINA AND MITRAL VALVE REGURGITATION	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	19APR10
0289	N0004852.0289.01	58	M	14OCT10	ANAEMIA	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	24SEP10
0296	N0000002.0296.01	72	M	23OCT10	FEVER 38.2 AND SUPRAPUBIC PAIN. ? URINARY TRACT INFECTION.	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	13OCT10
0032	N0000169.0032.01	62	M	23OCT10	INFLAMMATORY COLITIS	CONDITION STILL PRESENT AND UNCHANGED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	28MAY09
0235	N0000370.0235.02	81	F	01NOV10	RIGHT PLEURAL EFFUSION	RECOVERED WITH SEQUELAE	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	07DEC09
0033	N0000194.0033.01	74	M	30OCT10	DIABETES MELLITUS (TYPE 2)	RECOVERED WITH SEQUELAE	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	04AUG09
0027	N0000666.0027.02	46	F	25OCT10	ASTHMA ? SECONDARY TO IMATINIB	CONDITION STILL PRESENT AND UNCHANGED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	18MAY09
0214	N0000126.0214.01	62	M	23NOV10	BILATERAL PLEURAL EFFUSIONS	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	24APR10
0235	N0000370.0235.03	81	F	16NOV10	RIGHT PLEURAL EFFUSION RECURRENT	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	22JUN10
0319	N0000090.0319.01	83	F	26NOV10	CELLULITIS OF BOTH LEGS + LYMPHOEDEMA	RECOVERED WITH SEQUELAE	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	18NOV10
0243	N0000132.0243.02	79	F	02DEC10	PLEURAL EFFUSION	RECOVERED WITH SEQUELAE	DASATINIB	DASATINIB	50	MG	DAILY	ORAL	10AUG10
0320	N0000361.0320.01	67	M	01DEC10	LOW HAEMOGLOBIN	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	24NOV10
0096	N0000052.0096.01	62	M	29SEP10	BILATERAL PLEURAL EFFUSION	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	05OCT09

0100	N0000052.0100.01	55	M	17JAN11	PLEURAL EFFUSION NEEDING DRAINAGE	RECOVERED WITH SEQUELAE	DASATINIB	DASATINIB	50	MG	DAILY	ORAL	08OCT09
0160	N0000072.0160.01	48	M	25JAN11	CHEST PAIN	COMPLETELY RECOVERED	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	02FEB10
0068	N0000092.0068.01	33	M	21SEP09	PSYCHOLOGICAL DISTURBANCE	RECOVERED WITH SEQUELAE	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	18NOV10
0097	N0000039.0097.01	65	M	25DEC10	DIFFICULTY SWALLOWING	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	07OCT09
0294	N0000110.0294.01	55	M	12NOV10	NAUSEA/VOMITING	COMPLETELY RECOVERED	IMATINIB	IMATINIB	400	MG	DAILY	ORAL	10NOV10
0071	N0000218.0071.01	78	M	13APR11	DIARRHOEA + DEHYDRATION	CONDITION IMPROVING	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	14AUG09
0017	N0000006.0017.01	43	F	07MAR11	BREAST CANCER	CONDITION IMPROVING	DASATINIB	DASATINIB	40	MG	DAILY	ORAL	15APR09
0098	N0000175.0098.01	60	M	03APR11	QUERY CHEST INFECTION, PNEUMONIA, RIGHT PLEURAL EFFUSION	CONDITION IMPROVING	DASATINIB	DASATINIB	100	MG	DAILY	ORAL	08OCT09

 Indicates a SAR reported in a previous safety report

3 Aggregate summary tabulation of suspected SARs

Not applicable