Academic Haematology
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21 June 2010

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

Please find on the enclosed CD 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 (Dr S G O'Brien) or myself.

Yours sincerely,

C. Hedgley

Corinne Hedgley
Senior Trial Project Manager.

cc Amanda Tortice
R&D Manager, Newcastle-upon-Tyne Hospitals 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	Dr S. G. O'Brien
SPONSOR	Newcastle upon Tyne Hospitals Trust
Reporting Period	April 2009 – April 2010

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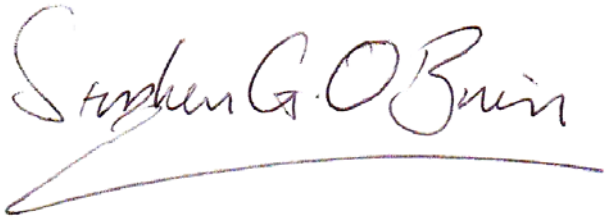

21 June 2010

Dr 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 2009 to April 2010) there were no SUSARs and 14 SARs reported to the sponsor.

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

The study team have recognised that there is a higher SAE/SAR reporting rate in the Dasatinib arm. We are monitoring this carefully but believe it probably to be 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 3 reports (1 serious) of pleural effusion to-date on the dasatinib arm (none on the imatinib arm). The study team are actively monitoring reports of suspected plural effusions. The Dasatinib SmPC lists pleural effusions as 'very common'; we are monitoring these closely to ensure the reporting in this study is no higher than expected rate (7% of patients).

The safety data were reviewed by the study DMC on the 17th May 2010. 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 DIASTOLLIC 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

Indicates a SAR reported in a previous safety report

3 Aggregate summary tabulation of suspected SARs

Not applicable