

**SPIRIT 2 CLINICAL TRIAL SUPPLIES  
INFORMATION FOR PHARMACISTS**

**SPIRIT 2**

A phase III, prospective randomised comparison of  
**- imatinib 400mg daily**  
 versus  
**- dasatinib 100mg daily**  
 in patients with newly-diagnosed chronic phase chronic myeloid leukaemia  
 (CML).

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## About SPIRIT 2

- SPIRIT 2 is a Phase III, multicentre, open-label, prospective randomised trial comparing imatinib (Glivec) 400 mg daily versus dasatinib (Sprycel) 100mg daily in patients with newly-diagnosed chronic phase CML.
- The sample size is 810 patients (405 patients per arm).
- After screening, all patients will be randomised in equal proportions to one of the following three treatment groups:
  - a) Imatinib 400 mg daily
  - b) Dasatinib 100 mg daily
- Both treatments will be started immediately at full dose.
- The primary endpoint is to compare Event Free Survival (EFS) at 5 years. Additional endpoints are defined in section 3 of the protocol.
- The Dasatinib will be provided free of charge by Bristol Myers Squib (BMS) for at least 5 years per patient. There is therefore a net saving of NHS treatment costs of up to 5 years of imatinib for 50% of entrants.
- Further details about the study can be found at [www.spirit-cml.org](http://www.spirit-cml.org)

## Study Medication

Further information can be found in section 8 of the protocol

### Imatinib

**Arm A:** The 400mg daily imatinib is supplied from your hospitals own NHS stock.

### Dasatinib

**Arm B:** The 100mg daily Dasatinib will be provided free of charge by Bristol Myers Squib for at least 5 years per patient.

The free Dasatinib supply is guaranteed for 5 years for each patient from the point at which the last patient is randomised into the trial – representing a minimum of 5 years supply per patient at least. After that point a continuing supply of free drug may be agreed with BMS but if this is not possible it is up to your hospital to decide what their continuing care should be.

One possible exit strategy is that patients remaining on study at 5 years on SPIRIT Arms B will revert to the NICE approved regime of 400 mg daily imatinib.


- Clinical Trial Supplies of dasatinib 50mg and 20 mg film coated tablets will be supplied in bottles of 30 tablets directly from BMS.
- Storage
  - Store at 15 - 25°C.

## Labelling

### Imatinib

Clinical Trial Labels will need to be applied to the NHS-supplied imatinib commercial stock used for the study. The labels will be supplied by the Trial Office. The following information will need to be added to the label in the pharmacy: Investigator, Site number, Patient Initials and Trial number and Date of dispensing.

Example of label:

For clinical trial use only. Keep out of reach of children.	
	
<b>SPIRIT 2</b> EudraCT no. : <b>2007-006185-15</b>	
Chief Investigator: Dr S. G. O'Brien.	
Trial Sponsor: The Newcastle-upon-Tyne Hospitals NHS Trust.	
For oral use only. To be used as directed by your doctor.	
Do not store above 30°C.	
Investigator: _____	Patient No.: _____
Site ID: _____	
Date Dispensed: _____	Patient Initials: _____

Additional labels should be requested from the trial manager.

### Dasatinib

The dasatinib will be provided with a multi-country clinical trial label (appendix 1) and a label identifying the trial and Sponsor (appendix 2). A local pharmacy label will need to be applied to identify the site, patient and date of dispensing. These can also be obtained from the Trial if required.

## Trial Prescriptions

Trial prescriptions are available on the SPIRIT website ([www.spirit-cml.org](http://www.spirit-cml.org)) in the SPIRIT 2 Pharmacy section. The prescription can be used as is or can be modified to suit practices at your site.

## Dose Reductions

For the management of toxicities the following dose reductions are allowed by the protocol. See protocol section 7 for further details.

Dosing Level Code	A 400mg daily imatinib	B 100mg daily dasatinib
	Total daily Imatinib (mg)	Total daily dasatinib (mg)
<b>1</b>	300*	50*
<b>2</b>	400	80*
<b>3</b>		100

(\*only used for managing toxicities)

## Returns and Destruction

Unused Study Drug should be returned to your hospital and destroyed following your normal hospital procedures.

Drug returns and destruction should be documented in the drug accountability log for the study file. A certificate of destruction should be sent to the trial manager where applicable.

## Pharmacy Documentation

As a minimum, the following pharmacy-related documentation will need to be kept for the study file.

- Drug Storage Conditions:
  - Document where and how drug will be stored at your site.
  - Document any monitoring systems that are used at your site that will apply to study drug stored at the site.
  - Document any deviations (eg. Temperature) that occur outside the recommended storage conditions for each product and how they were handled.
- Drug Dispensing>Returns/Destruction:
  - A log should be kept of all clinical trial supplies received by the pharmacy.

- A log should be kept of all drugs dispensed, returned and destroyed for the study
- Drug Dispensing and Returns Logs are available on the SPIRIT website in the Pharmacy Section
- A certificate of destruction should be sent to the trial manager where applicable.
- Labelling QC process:
  - Document how the labelling of the NHS stock imatinib will be QC'd or reference the relevant hospital procedure.

## **Drug Supply Flow**

Dasatinib for the SPIRIT 2 trial is sent directly from the manufacturer (BMS) to your pharmacy.

Drug supply is ordered for your site by the trial manager when certain criteria and study time points are met. These are detailed below.

**Please ensure that the Trial Office? has the correct pharmacy details (contact, address etc) for your site.**

### **Site Activated**

- When your hospital has received local Trust R&D and local ethics approval your site will be activated. This allows your hospital to begin enrolment of patients into the trial.
- Upon site activation the trial manager will send some trial drug labels to your pharmacy and a float supply of dasatinib 6 bottles of 50mg tablets and 6 bottles of 20mg tablets will be ordered.

### **Patient Randomised to dasatinib<sup>100</sup>**

- When a patient is randomised to the dasatinib arm the trial team will automatically order 6 bottles of 50 mg tablets for your hospital.

### **Patient Continuing in Trial**

- For patients continuing on treatment please complete the dasatinib order form when you require resupply stating the number of bottles of dasatinib required at each strength. The order form can be found on the SPIRIT website – Documents and Downloads - Pharmacy Section.



# SPIRIT2

STI571 Prospective International Randomised Trial

## Contents of SPIRIT 2 Pharmacy Pack

The documents listed below can all be found on the SPIRIT 2 Pharmacy section of the SPIRIT website <http://www.spirit-cml.org/SPIRIT 2/Pharmacy Section>

- Information for Pharmacists (this document)
- Drug Dispensing and Returns Log
- Study Drug Receipt Log
- Trial Prescriptions
- Dasatinib certificates of analysis
- Dasatinib Order Form
- Imatinib SmPC
- Dasatinib Investigators Brochure

Clinical Trial Labels for the imatinib will be sent to your pharmacy by the SPIRIT Trial Project Manager.

## **SPIRIT Assistant Trial Manager Contact Details**

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Website: [www.spirit-cml.org](http://www.spirit-cml.org)

**Appendix 1 - Dasatinib Multi-country Labels**

<http://www.spirit-cml.org/SPIRIT 2/Pharmacy Section/Dasatinib Label 50mg>

<http://www.spirit-cml.org/SPIRIT 2/Pharmacy Section/Dasatinib Label 20mg>

**Appendix 2 – Datatinib study specific label**

<http://www.spirit-cml.org/SPIRIT 2/Pharmacy Section/Dasatinib SPIRIT 2 Label>