EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

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# Short Study Report for Health Authorities

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| **Name of Sponsor/Company: EORTC**<br>**Name of the finished product**<br>**Name of Active Ingredient** | Individual study Table Referring to Part of the Dossier<br><br>Volume:<br><br>Page | *(For National Authority Use Only)* |
| **Title of the Study** | A phase III randomised study evaluating surgery of residual disease in patients with metastatic gastro-intestinal stromal tumor responding to Imatinib mesylate Version 1.1, 22/9/2008 | |
| **Investigators & Study Centres** | S. Bonvalot, I. Gustave Roussy 114, rue Edouard Vaillant, 94805 VILLEJUIF CEDEX, France — Total 2 (16.7%)<br>B Bui-Nguyen, Institut Bergonie, 229 cours de l'Argonne, 33076 Bordeaux, France — 1 (8.3%)<br>F Van Coevorden, N.K.I / A.V.L. Plesmanlaan 121 1066 CX Amsterdam, Netherlands — 3 (25%)<br>S. Sleijfer, U.Z.Rotterdam, Dr. Molenwaterplein 40, PO box 2040, 3015 GD Rotterdam, Netherlands — 1 (8.3%)<br>AJ Gelderblom, Univ Med Ctr Leiden, Albinusdreef 2 - Postbus 9600, 2300 RC Leiden, Netherlands — 1 (8.3%)<br>T. De Pas, Istituto Europeo di Oncologia, Via Ripamonti, 435, 20141 Milano, Italy — 1 (8.3%)<br>M. Leahy, The Christie NHS Foundation Trust, Wilmslow Road, M20 4BX Manchester, United Kingdom — 2 (16.7%)<br>A Gronchi, IRCCS - Fondazione Istituto Nazionale dei Tumori, Via Giacomo Venezian, 1, 20133 Milano, Italy — 1 (8.3%)<br>Total — 12 | |
| **Publication (reference)** | There was no publication for this study which was closed for poor accrual with small number of patients registered | |
| **Phase of development** | *Phase 3* | |

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| **Studied period** | Date of first enrolment: 20/05/2009<br>Date of last enrolment: 21/09/2010<br>Clinical cut-off date: 13/01/2011<br>*Date of early termination, if any:* 2011-03-11 | |
| **Substantial changes to the protocol** | *NA* | |
| **Objective(s)** | Primary: to evaluate whether surgery of residual disease in patients with advanced GIST responding to imatinib improves the progression free survival.<br>Secondary: to correlate the pharmacokinetics of imatinib and its metabolites in both the experimental (surgery) and standard (non-surgery) treatment arms, with the pharmacokinetics of imatinib and metabolites preceding randomisation. | |
| **Methodology** | This is a randomized multicenter phase III comparison trial<br>Eligible patients will be randomized after 6 to 12 months from starting molecular-targeted therapy with imatinib for metastatic disease, either as a standard of care, or within other clinical studies, to receive surgery of residual disease (investigational arm) or not. | |
| **Number of patients**<br>Number planed (Statistical design)<br>Number analysed | 350 patients will be included in this trial<br>12 | |
| **Diagnosis and main criteria for inclusion** | ¨ Histologically confirmed GIST expressing CD117+, or with documented mutation of the KIT or PDGFRA gene<br>¨ Metastatic disease (liver and/or abdominal cavity); no extra-abdominal metastases<br>¨ Treatment with imatinib administered for 6-12 months, resulting in CR, PR or SD, without PD since the start of Imatinib therapy (RECIST)<br>¨ No prior treatment with imatinib or other tyrosine kinase inhibitors (for any reason) in the adjuvant or neoadjuvant setting<br>¨ Measurable disease (RECIST) before start of imatinib<br>¨ Surgically resectable residual disease (assessed on CT scan/ MRI)<br>¨ Age ≥ 18 years; performance status 0 to 1 (WHO scale)<br>¨ Adequate hematologic and organ function | |

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| **Treatment** Test product, dose and mode of administration (batch number if applicable) Duration of treatment | Patients allocated to the investigational arm will be operated within the 12th month from imatinib onset. Postoperative imatinib treatment will be restored as soon as possible after surgery. | |
| **Reference therapy,** dose and mode of administration (batch number if applicable) | Patients allocated to the standard arm will continue imatinib treatment (according to standard practice) | |
| **Criteria for evaluation** | | |
| Efficacy | Primary: PFS measured from the date of randomization<br>Secondary: OS measured from the date of randomization; PFS and OS measured from the start of imatinib therapy<br>Pathological response to imatinib (in the surgery arm) | |
| Safety | Surgical morbidity (in the surgery arm) | |
| **Statistical methods** | PFS and OS from randomization will be analyzed in the intent to treat population (all randomized patients), using Kaplan-Meier estimates and logrank tests.<br>Analysis of PFS and OS from start of imatinib, pathological response to imatinib (in the surgery arm) and morbidity will be descriptive only. | |

**Summary of Results**

Efficacy Results

Baseline characteristics

Gender

| | Surgery | Control arm |
|---|---|---|
| Male | 3 (50%) | 4 (66.7%) |
| Female | 3 (50%) | 2 (33.3%) |
| Total | 6 | 6 |

Age

| | Surgery | Control arm |
|---|---|---|
| <50 | | 1 (16.7%) |
| >=50 | 6 (100%) | 5 (83.3%) |
| Total | 6 | 6 |

Site of Primary

| | Surgery | Control arm |
|---|---|---|
| Retro-intra abdominal | | 1 (16.7%) |
| Visceral Gastro Intestinal | 6 (100%) | 5 (83.3%) |
| Total | 6 | 6 |

Performance Status

| | Surgery | Control arm |
|---|---|---|
| 0 | 5 (83.3%) | 4 (66.7%) |
| 1 | 1 (16.7%) | 2 (33.3%) |
| Total | 6 | 6 |

Site of Metastatic disease

| | Surgery | Control arm |
|---|---|---|
| Liver | 5 (83.3%) | 3 (50%) |
| Abdominal cavity | 1 (16.7%) | 1 (16.7%) |
| Liver + abdominal cavity | | 2 (33.3%) |
| Total | 6 | 6 |

Subsite of disease

| | Surgery | Control arm |
|---|---|---|
| Small bowel | 2 (33.3%) | 3 (50%) |
| Gastric | 3 (50%) | 2 (33.3%) |
| Rectum | 1 (16.7%) | |
| Abdomen | | 1 (16.7%) |
| Total | 6 | 6 |

Safety Results

1 SAE reported: Localised intraabdominal fluid collection

Conclusions

This study was closed for poor accrual with a total number of 12 patients. A formal statistical analysis is not possible due to lack of data;

**Date of Report** 13/01/2011