



Clinical trial results:

A randomised phase II study of sunitinib versus dacarbazine in the treatment of patients with metastatic uveal melanoma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2008-008794-55 |
| Trial protocol | GB |
| Global end of trial date | 17 March 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 28 February 2019 |
| First version publication date | 28 February 2019 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | RDD299 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|----------------|
| ISRCTN number | ISRCTN75033520 |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | The Clatterbridge Cancer Centre NHS Foundation Trust |
| Sponsor organisation address | Clatterbridge Road, Wirral, United Kingdom, CH63 4JY |
| Public contact | Ms Charlotte Rawcliffe, Liverpool Cancer Trials Unit, University of Liverpool, 0151 794 8167, C.Rawcliffe@liverpool.ac.uk |
| Scientific contact | Dr Victoria Shaw, GCLP Labs, University of Liverpool, 0151 706 4180, Victoria.Shaw@liverpool.ac.uk |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 June 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 November 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 March 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Can the progression free survival time of patients with metastatic Uveal Melanoma be extended by treatment with Sunitinib, compared with the treatment by Dacarbazine?

Protection of trial subjects:

Consent should be obtained prior to each patient participating in the trial, after a full explanation has been given of the treatment options, including the conventional and generally accepted methods of treatment. The right of patients to refuse their consent to participate in the trial without providing a reason must be respected.

Verification of appropriate informed consent will be enabled by the provision of copies of participants' signed informed consent form being supplied to the LCTU by recruiting centres. This requires that name data will be transferred to the LCTU, which is explained in the PIS. The LCTU will preserve the confidentiality of participants taking part in the study and the University of Liverpool is a Data Controller registered with the Information Commissioners Office.

Individual participant medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. CRFs will be labelled with patient initials and unique trial screening and/or randomisation number. Blood and paraffin blocks will be transferred to the LECMC GCLP laboratory and will be identifiable by unique trial randomisation number only. Consent forms sent to the LCTU as part of the randomisation process may contain patient identifiers for the purpose of monitoring as described in the trial risk assessment. Such information will be stored in secure, locked cabinets.

The LCTU will request consent from all patients to obtain information from the NHS Information Centre (Medical Research Information Service) to follow patient progress if this is not available from their hospital or General Practitioner (GP).

Background therapy: -

Evidence for comparator:

Relapsed uveal melanoma carries a dismal prognosis and to date no systemic or regional therapy has shown a survival advantage over best supportive care. As a consequence there is an urgent need to investigate novel therapies in this disease. Presently, patients with metastatic uveal melanoma have few treatment options given the limited available evidence base for systemic therapy. In the UK, the majority of patients are managed with symptomatic measures, DTIC chemotherapy or entry into phase I clinical programmes.

Preliminary evidence suggests that C-Kit and angiogenesis may both play a role in disease progression and that Imatinib may have limited activity irrespective of C-Kit expression.

Sunitinib is a multi-targeted TKI which has shown significant activity both in Imatinib resistant GIST but also in a range of malignancies by virtue of its anti-angiogenic effects. A preliminary report of efficacy in uveal melanoma requires confirmation in a larger randomised controlled setting.

The heterogeneous nature of the disease and variable prognosis according to tumour volume at relapse limit the utility of further small single arm pilot phase II studies.

Currently, DTIC represents a standard of care in the absence of evidence based protocols and thus Sunitinib will be investigated in a randomised phase II setting with the opportunity for cross-over on first progression. For the purposes of this trial and potential future phase III comparison, DTIC will be administered at an internationally recognised standard dose of 1000mg/m².

| | |
|---|-----------------|
| Actual start date of recruitment | 22 October 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 84 |
| Worldwide total number of subjects | 84 |
| EEA total number of subjects | 84 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 48 |
| From 65 to 84 years | 36 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

UK; First patient randomised: 22/10/2010; Last patient randomised: 07/08/2012;

Cut off date: 30/11/2012;

Total number randomised to Cutoff date: 84

Total number withdrawn from study to Cutoff date: 75/84 before crossover (62 due to progression); 19/35 after crossover (12 due to progression)

Total number of deaths to Cutoff date: 54

Pre-assignment

Screening details:

ECOG performance status (see Appendix B); Physical Examination (including weight); Urine pregnancy test; 12 lead ECG; Vital Signs; Haematology; Biochemistry; CT scan; Additional MRI Scan; Identification of target lesions; CT Scan; Blood Sample

Cutoff date: 30/11/2012 - Total number screened to Cutoff date: 110

Period 1

| | |
|------------------------------|----------------------------------|
| Period 1 title | Treatment Phase (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Dacarbazine |

Arm description:

Patients will receive 1000mg/m² every 21 days by IV until progression or unacceptable toxicity

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Dacarbazine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dacarbazine will be administered as an open-label by IV infusion 1000mg/m² over 30 to 60 minutes, starting on Week 1 and repeated every 3 weeks until disease progression or unacceptable toxicity.

| | |
|------------------|-----------|
| Arm title | Sunitinib |
|------------------|-----------|

Arm description:

Sunitinib 50mg to be taken orally once a day for 28 days followed by 14 day break, until progression or unacceptable toxicity.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sunitinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Individual patients will receive 28 days supply, dispensed at every other 3-weekly clinic visit (i.e. every 6 weeks) according to locally defined policy.

50mg of Sunitinib to be taken by mouth once a day for 28 days followed by a 14 day break (4/2 schedule) until progression or unacceptable toxicity.

| Number of subjects in period 1 | Dacarbazine | Sunitinib |
|---|-------------|-----------|
| Started | 40 | 44 |
| Cross Over | 24 | 11 |
| Completed | 24 | 11 |
| Not completed | 16 | 33 |
| Withdrew between cross-over of treatments | 16 | 33 |

Baseline characteristics

Reporting groups

| | |
|--|-------------|
| Reporting group title | Dacarbazine |
| Reporting group description: | |
| Patients will receive 1000mg/m ² every 21 days by IV until progression or unacceptable toxicity | |
| Reporting group title | Sunitinib |
| Reporting group description: | |
| Sunitinib 50mg to be taken orally once a day for 28 days followed by 14 day break, until progression or unacceptable toxicity. | |

| Reporting group values | Dacarbazine | Sunitinib | Total |
|--|--------------|--------------|-------|
| Number of subjects | 40 | 44 | 84 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| median | 62.6 | 66.6 | |
| inter-quartile range (Q1-Q3) | 53.1 to 68.1 | 59.4 to 71.9 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 26 | 20 | 46 |
| Male | 14 | 24 | 38 |
| ECOG Performance | | | |
| ECOG Performance Status | | | |
| Units: Subjects | | | |
| ECOG 0 | 22 | 27 | 49 |
| ECOG 1 | 18 | 14 | 32 |
| ECOG 2 | 0 | 3 | 3 |

Subject analysis sets

| | |
|----------------------------|-------------------|
| Subject analysis set title | Full Analysis Set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

In order to follow the Intention to Treat (ITT) principle this will consist of all randomised patients excepting for:

- a) patients withdrawing consent between randomisation and starting therapy
- b) patients withdrawn from the study after randomisation because of irregularities with the consent process

c) patients whose information determining ineligibility existed before randomisation but was not read until after randomisation.

| | |
|--|-----------------|
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All patients who received any trial treatment. | |

| Reporting group values | Full Analysis Set | Safety Set | |
|---|-------------------|------------|--|
| Number of subjects | 84 | 84 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous | | | |
| Units: years | | | |
| median | | | |
| inter-quartile range (Q1-Q3) | | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 46 | 46 | |
| Male | 38 | 38 | |
| ECOG Performance | | | |
| ECOG Performance Status | | | |
| Units: Subjects | | | |
| ECOG 0 | 49 | 49 | |
| ECOG 1 | 32 | 32 | |
| ECOG 2 | 3 | 3 | |

End points

End points reporting groups

| | |
|---|-------------------|
| Reporting group title | Dacarbazine |
| Reporting group description: Patients will receive 1000mg/m ² every 21 days by IV until progression or unacceptable toxicity | |
| Reporting group title | Sunitinib |
| Reporting group description: Sunitinib 50mg to be taken orally once a day for 28 days followed by 14 day break, until progression or unacceptable toxicity. | |
| Subject analysis set title | Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: In order to follow the Intention to Treat (ITT) principle this will consist of all randomised patients excepting for: a) patients withdrawing consent between randomisation and starting therapy b) patients withdrawn from the study after randomisation because of irregularities with the consent process c) patients whose information determining ineligibility existed before randomisation but was not read until after randomisation. | |
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All patients who received any trial treatment. | |

Primary: Progression Free Survival

| | |
|--|---------------------------|
| End point title | Progression Free Survival |
| End point description: Progression will be defined according to Response Evaluation Criteria In Solid Tumours (RECIST) version 1.1 (see Appendix C) and will be captured by 12 weekly imaging, or imaging in the event of a clinical deterioration. Patients still alive with no evidence of progression at the time of their last visit are censored at the time of the most recent information. That is, PFS (months) = (min(censoring date, date of death) – date of randomisation)/30.4. The protocol specified that the analysis would take place once all patients have been followed up for at least 3 months. Because of the early termination (which might affect willingness to switch treatments) a common administrative censoring date was taken as the date of the TSC letter suspending randomisation (referred to as the “cutoff” date). Time to progression on firstline treatment (TTP1) will be compared to time to progression on secondline treatment (TTP2) for patients who receive crossover therapy | |
| End point type | Primary |
| End point timeframe: Measured as days from randomisation to progression or death. | |

| End point values | Dacarbazine | Sunitinib | Full Analysis Set | |
|----------------------------------|------------------|------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 40 | 44 | 84 | |
| Units: Subjects | | | | |
| median (confidence interval 95%) | 2.8 (2.6 to 2.9) | 2.8 (2.6 to 3.5) | 2.8 (2.6 to 2.9) | |

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | PFS Analysis |
| Comparison groups | Dacarbazine v Sunitinib |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7658 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 1.39 |

Secondary: AEs

| | |
|--|-----------|
| End point title | AEs |
| End point description: Classified using the NCI CTCAE version 4. Measured as the number of patients to experience at least 1 grade 3 adverse event. | |
| End point type | Secondary |
| End point timeframe: AEs experienced following randomisation | |

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | Dacarbazine | Sunitinib | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 44 | | |
| Units: Subjects | 27 | 23 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival of Crossover Patients

| | |
|-----------------|---|
| End point title | Progression Free Survival of Crossover Patients |
|-----------------|---|

End point description:

Time to progression on first-line treatment (TTP1) compared to time to progression on second-line treatment (TTP2) for patients who receive cross-over therapy

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Measured as days from randomisation to progression or death

| End point values | Dacarbazine | Sunitinib | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 44 | | |
| Units: Subjects | | | | |
| median (full range (min-max)) | 2.5 (0 to 12) | 2.5 (0 to 12) | | |

Statistical analyses

| Statistical analysis title | Second-line PFS |
|---|-------------------------|
| Comparison groups | Dacarbazine v Sunitinib |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 2.28 |

Secondary: Overall survival to death from any cause

| | |
|-----------------|--|
| End point title | Overall survival to death from any cause |
|-----------------|--|

End point description:

Patients known to have survived past the cutoff date (eg have attended for assessment after the cutoff date) will be censored at the cutoff date. Patients not known to have died but who have no record of attendance after the cutoff date will censored at the last visit date before the cutoff date.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Overall survival measured as months from randomisation to death from any cause

| End point values | Dacarbazine | Sunitinib | Full Analysis Set | |
|----------------------------------|-------------------|------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 40 | 44 | 84 | |
| Units: Subjects | | | | |
| median (confidence interval 95%) | 7.4 (6.2 to 11.1) | 6.3 (3.3 to 8.4) | 7.4 (6.1 to 8.4) | |

Statistical analyses

| Statistical analysis title | OS Analysis |
|---|-------------------------|
| Comparison groups | Dacarbazine v Sunitinib |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.208 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 2.61 |

Secondary: Overall response according to RECIST

| | |
|------------------------|--|
| End point title | Overall response according to RECIST |
| End point description: | Overall response rate on first-line treatment (RR1) compared to overall response rate on second-line treatment (RR2) for patients who receive cross-over therapy |
| End point type | Secondary |
| End point timeframe: | From randomisation until cut-off date |

| End point values | Dacarbazine | Sunitinib | Full Analysis Set | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 40 | 44 | 84 | |
| Units: Subjects | 3 | 0 | 3 | |

Statistical analyses

| | |
|---|---------------------------|
| Statistical analysis title | Difference in ORR |
| Comparison groups | Dacarbazine v Sunitinib |
| Number of subjects included in analysis | 84 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.108 |
| Method | Fisher exact |
| Parameter estimate | Difference in Proportions |
| Point estimate | -0.075 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.16 |
| upper limit | 0.01 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were reported from first patient first visit until 28 days after the last study treatment was administered.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | CTCTAE |
|-----------------|--------|

| | |
|--------------------|---|
| Dictionary version | 4 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Dacarbazine |
|-----------------------|-------------|

Reporting group description:

Patients will receive 1000mg/m² every 21 days by IV until progression or unacceptable toxicity
This reporting group also includes patients who have crossed over to Dacarbazine from the original Sunitinib Arm

| | |
|-----------------------|-----------|
| Reporting group title | Sunitinib |
|-----------------------|-----------|

Reporting group description:

Sunitinib 50mg to be taken orally once a day for 28 days followed by 14 day break, until progression or unacceptable toxicity.

This also includes patients who have cross over from Dacarbazine

| Serious adverse events | Dacarbazine | Sunitinib | |
|--|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 51 (29.41%) | 10 / 68 (14.71%) | |
| number of deaths (all causes) | 26 | 28 | |
| number of deaths resulting from adverse events | | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fever | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 7 / 7 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Ascites | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic Pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleuritic Pain | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| infections and infestations - Other | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 68 (2.94%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| lung infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin infection | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Creatinine Increased | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GGT increased | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil Count increased | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| White blood cell decreased | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate Phosphatase increased | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycemia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Dacarbazine | Sunitinib | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 51 (78.43%) | 55 / 68 (80.88%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 10 / 68 (14.71%) | |
| occurrences (all) | 4 | 16 | |
| Thromboembolic event | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 2 | |
| General disorders and administration site conditions | | | |
| Edema limbs | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 4 / 68 (5.88%) | |
| occurrences (all) | 2 | 4 | |
| FATIGUE | | | |
| subjects affected / exposed | 23 / 51 (45.10%) | 34 / 68 (50.00%) | |
| occurrences (all) | 43 | 50 | |
| FEVER | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 2 / 68 (2.94%) | |
| occurrences (all) | 10 | 2 | |
| Flu like symptoms | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences (all) | 1 | 1 | |
| Localized edema | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| PAIN | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | 9 / 68 (13.24%) | |
| occurrences (all) | 7 | 10 | |
| General disorders and administration | | | |

| | | | |
|--|---------------------|-----------------------|--|
| site conditions - Other, specify subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 2 / 68 (2.94%) 2 | |
| Reproductive system and breast disorders | | | |
| Irregular menstruation subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Menorrhagia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Vaginal hemorrhage subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 4 / 68 (5.88%) 6 | |
| DYSPNEA subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 5 | 8 / 68 (11.76%) 10 | |
| Epistaxis subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 4 / 68 (5.88%) 5 | |
| Hiccups subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Productive cough subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders - Other, specify subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Bronchopulmonary hemorrhage subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |

| | | | |
|---|------------------------|------------------------|--|
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 68 (1.47%) 1 | |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 68 (1.47%) 3 | |
| Restlessness subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Agitation subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Investigations | | | |
| Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Alanine Aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 4 | 5 / 68 (7.35%) 8 | |
| Alkaline Phosphatase Increased subjects affected / exposed occurrences (all) | 6 / 51 (11.76%) 6 | 7 / 68 (10.29%) 9 | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 6 / 51 (11.76%) 8 | 10 / 68 (14.71%) 15 | |
| Creatinine Increased subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 68 (2.94%) 3 | |
| GGT increased subjects affected / exposed occurrences (all) | 16 / 51 (31.37%) 21 | 16 / 68 (23.53%) 22 | |
| Haemoglobin increased | | | |

| | | | |
|---|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Investigations - Other, specify subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 5 | 4 / 68 (5.88%) 4 | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 8 | 6 / 68 (8.82%) 9 | |
| neutrophil count decreased subjects affected / exposed occurrences (all) | 12 / 51 (23.53%) 22 | 6 / 68 (8.82%) 9 | |
| platelet count decreased subjects affected / exposed occurrences (all) | 9 / 51 (17.65%) 16 | 10 / 68 (14.71%) 22 | |
| WEIGHT LOSS subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 4 / 68 (5.88%) 5 | |
| white blood cell decreased subjects affected / exposed occurrences (all) | 10 / 51 (19.61%) 13 | 6 / 68 (8.82%) 10 | |
| Blood Bilirubin Increased subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 6 / 68 (8.82%) 7 | |
| Injury, poisoning and procedural complications | | | |
| Bruising subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 1 / 68 (1.47%) 1 | |
| Wound complication subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Venous injury subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Cardiac disorders | | | |

| | | | |
|---|-----------------|------------------|--|
| Atrial fibrillation subjects affected / exposed occurrences (all) Palpitations subjects affected / exposed occurrences (all) Sinus bradycardia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| | 1 | 1 | |
| | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| | 1 | 0 | |
| | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| | 0 | 1 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| | 1 | 0 | |
| | 3 / 51 (5.88%) | 13 / 68 (19.12%) | |
| | 3 | 16 | |
| | 2 / 51 (3.92%) | 2 / 68 (2.94%) | |
| | 2 | 3 | |
| | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| | 1 | 1 | |
| | 2 / 51 (3.92%) | 2 / 68 (2.94%) | |
| | 2 | 6 | |
| Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) Blood and lymphatic system disorders - Other, specify subjects affected / exposed occurrences (all) Febrile neutropenia subjects affected / exposed occurrences (all) Thrombotic thrombocytopenic purpura | 9 / 51 (17.65%) | 6 / 68 (8.82%) | |
| | 13 | 10 | |
| | 3 / 51 (5.88%) | 4 / 68 (5.88%) | |
| | 7 | 5 | |
| | 2 / 51 (3.92%) | 0 / 68 (0.00%) | |
| | 2 | 0 | |
| | | | |
| | | | |

| | | | |
|---|-----------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 2 / 68 (2.94%) 2 | |
| Eye disorders | | | |
| Eye disorders - Other, specify subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| photophobia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Distension subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 68 (1.47%) 1 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 51 (5.88%) 3 | 6 / 68 (8.82%) 7 | |
| CONSTIPATION subjects affected / exposed occurrences (all) | 7 / 51 (13.73%) 15 | 7 / 68 (10.29%) 8 | |
| DIARRHEA subjects affected / exposed occurrences (all) | 7 / 51 (13.73%) 8 | 12 / 68 (17.65%) 13 | |
| Dry mouth subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 68 (1.47%) 1 | |
| dyspepsia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 10 / 68 (14.71%) 10 | |
| Flatulence subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Gastroesophageal reflux disease subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 68 (2.94%) 2 | |
| Gastrointestinal disorders - Other, specify | | | |

| | | | |
|--|-----------------|------------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 68 (2.94%) | |
| occurrences (all) | 1 | 2 | |
| Gastrointestinal pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mucositis oral | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 11 / 68 (16.18%) | |
| occurrences (all) | 3 | 15 | |
| NAUSEA | | | |
| subjects affected / exposed | 8 / 51 (15.69%) | 19 / 68 (27.94%) | |
| occurrences (all) | 8 | 25 | |
| VOMITING | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | 8 / 68 (11.76%) | |
| occurrences (all) | 8 | 9 | |
| Oral pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 5 / 68 (7.35%) | |
| occurrences (all) | 0 | 5 | |
| Bloating | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 3 | |
| Hepatobiliary disorders | | | |
| Hepatic pain | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 68 (1.47%) | |
| occurrences (all) | 2 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 68 (2.94%) | |
| occurrences (all) | 1 | 3 | |
| Erythema multiforme | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain of skin | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences (all) | 1 | 1 | |
| Palmar-plantar erythrodysesthesia syndrome | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences (all) | 1 | 1 | |
| Photosensitivity | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Scalp pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 68 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin atrophy | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 2 | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 2 | |
| Skin and subcutaneous tissue disorders - Other, specify | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 2 | |
| Nail discoloration | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 2 | |
| Skin hypopigmentation | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 68 (4.41%) | |
| occurrences (all) | 0 | 3 | |
| skin hyperpigmentation | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 4 / 68 (5.88%) | |
| occurrences (all) | 0 | 8 | |
| Renal and urinary disorders | | | |
| urinary tract pain | | | |

| | | | |
|---|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 2 / 68 (2.94%) 2 | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 68 (2.94%) 2 | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 51 (5.88%) 4 | 0 / 68 (0.00%) 0 | |
| Bone pain subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 2 | 2 / 68 (2.94%) 2 | |
| Flank pain subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Muscle weakness lower limb subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 68 (1.47%) 1 | |
| Myalgia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 68 (0.00%) 0 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 3 / 68 (4.41%) 3 | |
| Buttock pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 68 (1.47%) 1 | |
| Infections and infestations Infections and infestations - Other, specify subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 2 / 68 (2.94%) 2 | |
| lung infection | | | |

| | | | |
|------------------------------------|----------------|-----------------|--|
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences (all) | 1 | 1 | |
| Rhinitis infective | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 68 (1.47%) | |
| occurrences (all) | 1 | 1 | |
| urinary tract infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 68 (4.41%) | |
| occurrences (all) | 1 | 3 | |
| Mucosal infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| Eye infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| Upper respiratory infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| Bladder infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| ANOREXIA | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 8 / 68 (11.76%) | |
| occurrences (all) | 6 | 10 | |
| HYPOALBUMINEMIA | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 2 / 68 (2.94%) | |
| occurrences (all) | 5 | 3 | |
| Hypokalemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 68 (2.94%) | |
| occurrences (all) | 1 | 2 | |
| HYPONATREMIA | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 5 / 68 (7.35%) | |
| occurrences (all) | 4 | 6 | |
| HYPOPHOSPHATEMIA | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 68 (1.47%) | |
| occurrences (all) | 2 | 1 | |

| | | | |
|-----------------------------|----------------|----------------|--|
| Dehydration | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| Hyperkalemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| Hypocalcemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 3 | |
| Hypercalcemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| HYPOMAGNESEMIA | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 68 (1.47%) | |
| occurrences (all) | 0 | 1 | |
| HYPERNATREMIA | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 68 (2.94%) | |
| occurrences (all) | 0 | 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 28 July 2010 | AMENDMENT 1 (Substantial 01) - Addition of sites (Beatson, Royal Devon & Exeter, Southampton, The Christie) - Change in PI (Royal Marsden) - Change of Institution (Hillingdon to East & North Hertfordshire) |
| 02 November 2010 | AMENDMENT 2 (Substantial 02) - Update to protocol (Version 1 to 2) * Inclusion criteria changes: to refer to randomisation correct units for platelets (Section 2 pages 12-13, Section 6 24-25) * Exclusion criteria changes: typographical error corrected reference to Coumadin removed (Section 2 pages 12-13, Section 6 24-25) * Trial Schematic updated: to reflect protocol changes (Section 2 15-16) * Clarification of withdrawal process (section 6.3 page 25, section 6.3.2 page 26) * Enrolment and randomisation details clarified (section 7, page 27-28) |
| 17 May 2011 | AMENDMENT 3 (Substantial 03) - Addition of New Site (Queen Elizabeth, Birmingham) |
| 07 June 2012 | AMENDMENT 4 (Substantial 04) - Addition of New Site (Velindre) |
| 30 August 2012 | AMENDMENT 5 (Substantial) - Change of Sponsor name (Clatterbridge Centre for Oncology NHS Foundation Trust to The Clatterbridge Cancer Centre NHS Foundation Trust) |
| 14 December 2012 | AMENDMENT 6 (Substantial 05) - Protocol update (Version 2 to Version 3) * Administrative updates to trial management (adding new contacts, clearer instructions for dose modification and RECIST 1.1) * Expansion of window for Tumour Assessments (+/- 2 weeks rather than +/- 1 week) * Updated central monitoring procedures (closer monitoring of our primary endpoint of PFS by requesting CT scan reports be sent in to LCTU at all time points as previously only requested at Crossover) * Allowance for Dacarbazine administration in elderly patients (at PI discretion, can start at 850 mg/m2 rather than 1000mg/m2) * Updating inclusion criteria from transaminases < 5 x ULN to AST and ALT < 5 x ULN - PIS update (Version 2 to Version 3) - GP Letter update (Version 2 to Version 3) - Addition of New Site (St Barts) |
| 07 January 2013 | AMENDMENT 8 (Substantial 06) - Cessation to recruitment - Addendum to ICF Version 1 and Addendum to PIS Version 1 (explaining cessation of recruitment) |
| 02 July 2013 | AMENDMENT 9 (Substantial 07) - Update from Protocol Version 3 to Version 4 * Addition of a specific reference to the RSI to the Pharmacovigilance section - Changes in PI (Leicester and Weston Park) |
| 05 September 2013 | AMENDMENT 11 (Substantial 08) - Update to the Sunitinib SmPC Version 4 to Version 5 |

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| 04 February 2014 | <p>AMENDMENT 12 (Substantial 09)</p> <ul style="list-style-type: none"> - Update to Protocol Version 4 to Version 5 (update to the End of Trial definition - 'If trial recruitment ends early due to harm or futility the end of trial will be 28 days after the first progression of the last patient currently treated with sunitinib, or 28 days after the second progression of the last patient currently treated with Sunitinib, whichever is later.') - End date changed to 01/11/2014 (The study end date was amended to 22/10/2013. That date passed and there were still some patients receiving Sunitinib, therefore an extension to the study end date was required for patient to reach the end of trial under the definition above.) |
|------------------|--|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported