



Clinical trial results: Phase II Study of Imatinib Mesylate for Philadelphia-Positive Acute Lymphocytic Leukemia Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-001805-34 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 14 February 2007 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 26 July 2018 |
| First version publication date | 26 July 2018 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CSTI571A1203 |
|-----------------------|--------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|----------------------------------------------------------------|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, |

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 | 14 February 2007 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 February 2007 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy and safety of STI571 in patients diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment | 07 May 2004 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------|
| Country: Number of subjects enrolled | Japan: 8 |
| Worldwide total number of subjects | 8 |
| EEA total number of subjects | 0 |

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) | 1 |
| Adults (18-64 years) | 5 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Treatment initiation day was expressed as Day 1 (the day before the treatment initiation as Day -1).
Screening were performed between Day -7 and Day -1 (the day before the treatment initiation).

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Core phase |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|---------------------------|
| Arm title | All subjects - Core phase |
|------------------|---------------------------|

Arm description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).
Core phase (up to 12 weeks): a remission induction therapy with STI571 was conducted in this phase.

| | |
|----------------------------------------|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | STI571 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

STI571: 600 mg (oral once daily); a dose may be increased up to 800 mg (400 mg oral twice daily) in patients with an inadequate response

| | |
|---------------------------------------|---------------------------|
| Number of subjects in period 1 | All subjects - Core phase |
| Started | 8 |
| Completed | 6 |
| Not completed | 2 |
| Inadequate response | 2 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Extension phase |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Arm title | All subjects - Extension phase |
| Arm description: 600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg). Extension phase (until the study completion): treatment with STI571 continues in responders. | |
| Arm type | Experimental |
| Investigational medicinal product name | STI571 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

STI571: 600 mg (oral once daily); a dose may be increased up to 800 mg (400 mg oral twice daily) in patients with an inadequate response

| Number of subjects in period 2 | All subjects - Extension phase |
|------------------------------------------------------|-----------------------------------|
| Started | 6 |
| Completed | 1 |
| Not completed | 5 |
| Difficulty in making office visits | 2 |
| No need to treat with the investigational product | 2 |
| Inadequate response | 1 |

Baseline characteristics

Reporting groups

Reporting group title

Core phase

Reporting group description: -

| Reporting group values | Core phase | Total | |
|-------------------------------------------------------|------------|-------|--|
| Number of subjects | 8 | 8 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 1 | 1 | |
| Adults (18-64 years) | 5 | 5 | |
| From 65-84 years | 2 | 2 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 51.6 | | |
| standard deviation | ± 16.7 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 5 | |
| Male | 3 | 3 | |

End points

End points reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | All subjects - Core phase |
|-----------------------|---------------------------|

Reporting group description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).

Core phase (up to 12 weeks): a remission induction therapy with STI571 was conducted in this phase.

| | |
|-----------------------|--------------------------------|
| Reporting group title | All subjects - Extension phase |
|-----------------------|--------------------------------|

Reporting group description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).

Extension phase (until the study completion): treatment with STI571 continues in responders.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Core + Extension phases |
|----------------------------|-------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All patients diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia.

Core phase (up to 12 weeks): a remission induction therapy with STI571 is to be conducted in this phase.

Extension phase (until the study completion): treatment with STI571 continues in responders.

Primary: Percentage of patients with Hematologic response (CHR + Marrow-CR)

| | |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Percentage of patients with Hematologic response (CHR + Marrow-CR) ^[1] |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

Complete hematologic response (CHR): peripheral blasts = 0%, bone marrow blasts <5%, neutrophils $\geq 1500/\text{mm}^3$, and platelets $\geq 100\,000/\text{mm}^3$ + Complete marrow response (Marrow-CR): peripheral blasts = 0% and bone marrow blasts <5%

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Antileukemic effect of STI571 monotherapy persisted for at least 4 weeks.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses have been reported for this primary endpoint.

| End point values | All subjects - Core phase | | | |
|----------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 ^[2] | | | |
| Units: Percentage of patients | | | | |
| number (confidence interval 95%) | | | | |
| All Response (n=8) | 100 (63.1 to 100.0) | | | |
| Sustained Response (n=5) | 62.5 (24.5 to 91.5) | | | |

Notes:

[2] - full analysis set (FAS)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with Cytogenetic response

| | |
|-----------------|--------------------------------------------------|
| End point title | Percentage of patients with Cytogenetic response |
|-----------------|--------------------------------------------------|

End point description:

Cytogenetic response (CGR):

Complete CGR: At least 1 confirmed elimination of Philadelphia chromosome

Major CGR: At least 1 confirmed suppression of Philadelphia chromosome to between 1% and 35%

End point type

Secondary

End point timeframe:

Antileukemic effect of STI571 monotherapy persisted for at least 4 weeks.

| End point values | Core + Extension phases | | | |
|----------------------------------|-------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 8 ^[3] | | | |
| Units: Percentage of patients | | | | |
| number (confidence interval 95%) | 87.5 (47.3 to 99.7) | | | |

Notes:

[3] - full analysis set (FAS); patients who reached the Cytogenetic response : n=7.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 7.0 |

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All subjects |
|-----------------------|--------------|

Reporting group description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).

Core phase (up to 12 weeks): a remission induction therapy with STI571 was conducted in this phase.

Extension phase (until the study completion): treatment with STI571 continues in responders.

| Serious adverse events | All subjects | | |
|---------------------------------------------------|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Puncture site hemorrhage | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral hemorrhage | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin rash | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| Sepsis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | All subjects | | |
|---------------------------------------------------------------------|-----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumor lysis syndrome | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Petechiae | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Haemorrhage | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Malaise | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Oedema | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | | |
| occurrences (all) | 4 | | |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Oedema peripheral | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Injection site reaction | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Puncture site haemorrhage | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Pharyngolaryngeal pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Pharynx discomfort | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract inflammation | | | |

| | | | |
|------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 4 / 8 (50.00%) 4 | | |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 3 / 8 (37.50%) 3 | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 2 | | |
| Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all) | 4 / 8 (50.00%) 4 | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 2 | | |
| Hemoglobin decreased subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Weight increased subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Urinary occult blood positive subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 2 | | |
| Hepatic enzyme increased | | | |

| | | | |
|------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Blood amylase increased | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| PH urine abnormal | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Laceration | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Nerve injury | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Burning sensation | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Dysgeusia | | | |

| | | | |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Headache | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Hypothymia | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Dizziness postural | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | | |
| occurrences (all) | 4 | | |
| Neutropenia | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Leukopenia | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Myelosuppression | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |

| | | | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|
| Lymphadenopathy subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Eye disorders Conjunctival hemorrhage subjects affected / exposed occurrences (all) Conjunctival edema subjects affected / exposed occurrences (all) Blepharitis subjects affected / exposed occurrences (all) Eyelid edema subjects affected / exposed occurrences (all) Lacrimation increased subjects affected / exposed occurrences (all) Photophobia subjects affected / exposed occurrences (all) Retinal haemorrhage subjects affected / exposed occurrences (all) | 4 / 8 (50.00%) 4 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 | | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain upper | 8 / 8 (100.00%) 8 5 / 8 (62.50%) 5 | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Constipation | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Cheilitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Gingival bleeding | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Faeces soft | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Oral discomfort | | | |

| | | | |
|----------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Periodontitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal mucosal disorder | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Hepatobiliary disorders | | | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 7 / 8 (87.50%) | | |
| occurrences (all) | 7 | | |
| Face edema | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | | |
| occurrences (all) | 4 | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Erythema | | | |

| | | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Keloid scar</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash vesicular</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 8 (12.50%)</p> <p>1</p> <p>1 / 8 (12.50%)</p> <p>1</p> <p>1 / 8 (12.50%)</p> <p>1</p> <p>1 / 8 (12.50%)</p> <p>1</p> | | |
| <p>Renal and urinary disorders</p> <p>Glomerulonephritis chronic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cystitis haemorrhagic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cystitis-like symptom</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 8 (12.50%)</p> <p>1</p> <p>1 / 8 (12.50%)</p> <p>1</p> <p>1 / 8 (12.50%)</p> <p>1</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Muscular weakness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Osteonecrosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 8 (50.00%)</p> <p>4</p> <p>1 / 8 (12.50%)</p> <p>1</p> <p>3 / 8 (37.50%)</p> <p>3</p> <p>1 / 8 (12.50%)</p> <p>1</p> | | |
| <p>Infections and infestations</p> | | | |

| | | | |
|-----------------------------|----------------|--|--|
| Neutropenic infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Sepsis | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | | |
| occurrences (all) | 4 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Dental caries | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Infection | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Catheter related infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Herpes simplex | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Herpes virus infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Perianal abscess | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Escherichia infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |

| | | | |
|------------------------------------|----------------|--|--|
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Hypoalbuminemia | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | | |
| occurrences (all) | 3 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | | |
| occurrences (all) | 5 | | |
| Fluid retention | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | | |
| occurrences (all) | 2 | | |
| Hypophosphatemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 07 June 2004 | Revision to clarify descriptions in inclusion and exclusion criteria and addition of on-site measurement methods to chromosome banding at screening were made. |
| 10 September 2004 | Changes in actions to be taken in case of occurrence of serious adverse events (SAE) were made in response to the revision of the clinical study standard operating procedures (SOP) of Novartis Pharma K.K. |
| 30 November 2004 | The study period was extended as treatment with the investigational product was likely to continue after April 2005. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Data which would be needed to produce non-SAE and SAE tables by programming, does not exist. SAE and non-SAE tables in this document are the data of serious ADR and all AE respectively. For full, disclosure, all data available has been reported.

Notes: