## Sponsor

Novartis

## Generic Drug Name

QAX576

## Therapeutic Area of Trial

Asthma

## Approved Indication

Investigational

## Study Number

CQAX576A2107

## Title

A randomized, double-blind, placebo-controlled study to compare the safety, tolerability, pharmacokinetics and pharmacodynamics of multiple doses of intravenous administration of QAX576 in controlled or partially controlled asthma patients

## Phase of Development

Phase I

## Study Start/End Dates

01 Jul 2009 to 15 Jan 2010

## Study Design/Methodology

This was a multiple center, randomized, double-blind, placebo controlled study in controlled or partially controlled asthmatic subjects. Doses of 1, 3, and 10 mg/kg of QAX576 were administered in a blinded fashion, 3 times, 21 days apart.

A total of 30 asthmatic patients were recruited, 10 to each cohort, 8 receiving QAX576 and 2 receiving placebo in each cohort. In total 28 subjects completed the study and two (3/5307, 1/5138) patients discontinued from the study due to an adverse event. All subjects were included for the safety and PD data analysis. Subjects were analyzed according to treatment received.

## Centers

The study was conducted at a total of five centers in the United Kingdom (1) and Russia (4)

## Publication

Not applicable

## Objectives

Primary objective(s)

To assess and to compare the safety and tolerability of multiple doses of QAX576 in controlled or partially controlled asthma patients.

Secondary objective(s)

- To assess the effect of QAX576 on asthma control using assessments such as exhaled NO, FEV1 variability data captured by PiKo®-1home monitoring device and the extent of inhaled salbutamol use as rescue medication.

## Test Product (s), Dose(s), and Mode(s) of Administration

QAX576 1 mg/kg,
QAX576 3 mg/kg,
QAX576 10 mg/kg.
Each treatment was administered a total of three times via i.v. infusion over a period of 2 hours, with each administration 21 days apart.

## Reference Product(s), Dose(s), and Mode(s) of Administration

Placebo administered a total of three times via i.v. infusion over a period of 2 hours, with each administration 21 days apart.

## Criteria for Evaluation

### Primary variables

Safety and tolerability assessing adverse events, vital signs, hematology, blood chemistry, urinalysis and ECG.

### Secondary variables

In-clinic spirometry assessments of FEV1, FVC and FEV% predicted, and also exhaled NO at days 1, 2, 22, 43, 64.

Home-monitoring diary data from the PiKo®-1devices for each dose period (days 3 through 21, days 23 through 42 and days 44 through 63, and if available days 65-91 assessing $FEV_1$ and as numbers (%) of subjects requiring rescue medication (none/some), by treatment group. Numbers of alerts (when $FEV_1$ drop is > 20% below baseline.

### Other

Pharmacogenetic: Optional blood sample was collected from each subject who agreed to participate in pharmacogenetic evaluations. Genetic assessments may be reported separately at a later date.

Biomarkers: Total IgE at day 1, 22, 43 and end of study. These assessments may be reported separately at a later date.

Anti-QAX576 antibody in serum.

## Statistical Methods

All patients as randomized that received at least one dose of study drug were included in the data analysis. Patients were analyzed according to treatment received. All subjects with evaluable pharmacodynamic (PD) parameter data will be included in the data analysis.

An interim analysis of safety and tolerability, and of spirometry data, was performed after all randomized patients who had completed 9 weeks on study following their first dose of QAX576 to enable planning for future studies with this compound.

For all summaries, data from placebo subjects were pooled across cohorts.

## Study Population: Inclusion/Exclusion Criteria and Demographics

### Inclusion criteria

1. Non-smoking male and female subject's age 18 to 65 years, inclusive; with controlled or partially controlled asthma those were otherwise healthy as determined by past medical history, physical examination, vital signs, electrocardiogram, and laboratory tests at screening. Female subjects were allowed to participate in this study if they were postmenopausal or surgically sterilized.

2. Controlled or partially controlled asthma as defined in GINA 2007 as follows:

| Characteristic | Controlled (All of the following) | Partially controlled (Any measure present in any week) |
|---|---|---|
| Daytime symptoms | None (twice or less/week) | More than twice/week |
| Limitations of activities | None | Any |
| Nocturnal symptoms/awakening | None | Any |
| Need for reliever/ rescue treatment | None (twice or less/week) | More than twice/week |
| Lung function (PEF or FEV1)‡ | Normal | < 80% predicted or personal best (if known) |
| Exacerbations | None | One or more/year* |

*Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

3. At Screening, and Baseline, vital signs (systolic and diastolic blood pressure and pulse rate) were assessed after the subject had rested for at least three (3) minutes. Vital signs were within the following ranges:

- oral body temperature between 35.0-37.5 °C
- systolic blood pressure, 90-140 mm Hg
- diastolic blood pressure, 50-90 mm Hg
- pulse rate, 40 - 90 bpm

All blood pressure measurements at other time-points were assessed with the subject seated and utilizing the same arm for each determination.

4. Female subjects were post-menopausal as confirmed by FSH $\geq$ 40, or were surgically sterilized at least 6 months prior to screening. Surgical sterilization procedures were supported with clinical documentation made available to sponsor and were noted in the Relevant Medical History/Current Medical Conditions section of the CRF.

5. Subjects must have a body mass index (BMI) within the range of 18 to 30 $kg/m^2$.

6. Male subjects were instructed for using two methods of contraception, i.e., spermicidal gel plus condom, for the entire duration of the study, up to Study Completion visit, and refrain from fathering a child in the six (6) months following last study drug administration.

7. Were able to communicate well with the investigator, to understand and comply with the requirements of the study. Understand and sign the written informed consent before any study specific procedure was performed.

## Exclusion criteria

Subjects meeting any of the following criteria were excluded from entry into the study:

1. Smokers (use of tobacco products in the previous 3 months). Urine cotinine levels were measured during screening and baseline for all subjects. Smokers were defined as any subject who reports tobacco use within the previous 3 months and had a positive urine cotinine according to local laboratory ranges. Individuals with a previous history of smoking (i.e. prior to the previous 3 months) not exceeding a 10 pack-year history.
2. Use of any prescription drugs other than stable (4 weeks) use of hormone replacement or thyroid replacement within four (4) weeks prior to dosing (other than medication required for treatment of asthma). Paracetamol was acceptable, but no more than 1g/day and was to be taken for no more than 3 of 7 days and documented in the Concomitant medications/Significant non-drug therapies page of the CRF.
3. Use of any over the counter (OTC) medication within forty eight (48) hours prior to dosing.
4. Use of oral steroids within 12 weeks prior to dosing.
5. Patients who had received an investigational drug in any clinical investigation within 4 weeks prior to dosing or longer if required by local regulations, and for any other limitation of participation based on local regulations.
6. Any immunotherapy with systemic biologics as a treatment therapy or during a clinical study with in the last 6 months.
7. Any immunotherapy with subcutaneous injections for allergy (allergy shots), within 3 months.
8. Donation or loss of 400 mL or more of blood within 8 weeks prior to first dosing, or longer if required by local regulation.
9. Clinically relevant illness within two weeks prior to dosing.
10. Patients suffering from hay fever at screening or likely to require treatment during the study.
11. A past medical history of clinically significant ECG abnormalities.
12. History of chronic respiratory disease other than asthma or chronic allergic rhinitis.
13. Emergency room visit within 6 weeks of screening due to asthma.
14. Hospitalization for asthma in the last year.
15. History of intubation/assisted ventilation for asthma in the last 5 years.
16. History of autonomic dysfunction (e.g. history of fainting, orthostatic hypotension).
17. History or presence of any surgical or medical condition or clinically significant abnormal laboratory findings, which, in the opinion of the investigator, would jeopardize the subject in case of participation in the study.
18. History of immunodeficiency diseases, including a positive HIV test result.
19. A positive Hepatitis B surface antigen (HBsAg) or Hepatitis C test result.
20. History of drug or alcohol abuse within the 12 months prior to dosing or evidence of such abuse as indicated by the laboratory assays conducted during the screening or baseline evaluations.
21. History of clinical schistosomiasis or travel within the preceding 6 months to an area with endemic schistosomiasis, including but not limited to Southeast Asia and Northwest Africa.
22. Positive stool sample for ova or parasites.

23. If blood absolute eosinophil count at screening ≥350 cells/$mm^3$, subjects were included in the study only after active parasitic infection was ruled out as the etiology of eosinophilia.

## Number of Subjects

| Disposition Reason | All subjects N=30 n (%) | -QAX576- 1 mg/kg N=8 n(%) | 3 mg/kg N=8 n(%) | 10 mg/kg N=8 n(%) | Placebo N=6 n(%) |
|---|---|---|---|---|---|
| **Patients** | | | | | |
| Randomized | 30 ( 100) | 8 ( 100) | 8 ( 100) | 8 ( 100) | 6 ( 100) |
| Completed | 28 (93.3) | 7 (87.5) | 8 ( 100) | 7 (87.5) | 6 ( 100) |
| Discontinued | 2 ( 6.7) | 1 (12.5) | 0 ( 0.0) | 1 (12.5) | 0 ( 0.0) |
| **Main cause of discontinuation** | | | | | |
| Adverse Event(s) | 2 ( 6.7) | 1 (12.5) | 0 ( 0.0) | 1 (12.5) | 0 ( 0.0) |

## Demographic and Background Characteristics

| | | -QAX576- 1 mg/kg N=8 | 3 mg/kg N=8 | 10 mg/kg N=8 | Placebo N=6 | Total N=30 |
|---|---|---|---|---|---|---|
| Age (years) | Mean (SD) | 51.4 (14.41) | 38.3 (11.36) | 36.1 (9.80) | 48.8 (12.70) | 43.3 (13.34) |
| | Median | 58.0 | 36.5 | 33.0 | 51.5 | 41.0 |
| | Range | 29-65 | 23-57 | 25-57 | 25-62 | 23-65 |
| Gender-n(%) | Male | 3 (37.5%) | 8 (100%) | 7 (87.5%) | 3 (50.0%) | 21 (70.0%) |
| | Female | 5 (62.5%) | 0 (0.0%) | 1 (12.5%) | 3 (50.0%) | 9 (30.0%) |
| Race-n(%) | Caucasian | 8 (100%) | 8 (100%) | 8 (100%) | 6 (100%) | 30 (100%) |
| Ethnicity-n(%) | Hispanic/Latino | 0 (0.0%) | 1 (12.5%) | 0 (0.0%) | 0 (0.0%) | 1 (3.3%) |
| | Other | 8 (100%) | 7 (87.5%) | 8(100%) | 6 (100%) | 29 (96.7%) |
| Weight (kg) | Mean (SD) | 73.36 (8.438) | 77.98( 4.719) | 75.56 (9.712) | 68.48 (10.983) | 74.20 (8.805) |
| | Median | 75.50 | 78.65 | 74.35 | 64.25 | 75.60 |
| | Range | 56.0-83.0 | 69.8-83.3 | 61.7-89.3 | 58.0-84.0 | 56.0-89.3 |
| Height (cm) | Mean (SD) | 168.25 (10.292) | 174.16 (4.724) | 174.11 (7.901) | 170.68 (8.031) | 171.88 (7.993) |
| | Median | 167.00 | 174.50 | 174.35 | 170.75 | 173.25 |
| | Range | 153.0-187.0 | 167.0-179.9 | 157.0-181.7 | 160.0-179.5 | 153.0-187.0 |
| BMI (kg/m2) | Mean (SD) | 26.075 (3.6941) | 25.746 (1.8765) | 24.993 (3.3816) | 23.520 (3.5255) | 25.188 (3.1522) |
| | Median | 26.760 | 26.160 | 24.675 | 22.505 | 24.675 |
| | Range | 21.08-29.71 | 23.57-28.62 | 20.93-29.62 | 20.3-29.77 | 20.3-29.77 |

BMI = body mass index

## Primary Objective Result(s)

### Summary of safety data (adverse events)

| Body system | -QAX576- 1 mg/kg N=8 n(%) | 3 mg/kg N=8 n(%) | 10 mg/kg N=8 n(%) | Placebo N=6 n(%) | Total N=30 n(%) |
|---|---|---|---|---|---|
| Subjects with AE(s) | 1(12.5) | 8(100) | 5(62.5) | 3(50.0) | 17(56.7) |
| System organ class | | | | | |
| Infections and infestations | 0(0.0) | 4(50.0) | 2(25.0) | 2(33.3) | 8(26.7) |
| Respiratory, thoracic and mediastinal disorders | 0(0.0) | 4(50.0) | 1(12.5) | 2(33.3) | 7(23.3) |
| Injury, poisoning and procedural complications | 0(0.0) | 0(0.0) | 3(37.5) | 1(16.7) | 4(13.3) |
| Nervous system disorders | 0(0.0) | 3(37.5) | 0(0.0) | 1(16.7) | 4(13.3) |
| Gastrointestinal disorders | 0(0.0) | 1(12.5) | 1(12.5) | 1(16.7) | 3(10.0) |
| General disorders and administration site conditions | 0(0.0) | 2(25.0) | 0(0.0) | 1(16.7) | 3(10.0) |
| Musculoskeletal and connective tissue disorders | 0(0.0) | 1(12.5) | 0(0.0) | 1(16.7) | 2(6.7) |
| Cardiac disorders | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Eye disorders | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Investigations | 1(12.5) | 0(0.0) | 0(0.0) | 0(0.0) | 1(3.3) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 1(12.5) | 0(0.0) | 0(0.0) | 0(0.0) | 1(3.3) |
| Skin and subcutaneous tissue disorders | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |

## Secondary Objective Result(s)

**Summary of spirometry (PD analysis)**

| | | QAX576 1mg/kg N=8 | QAX576 3mg/kg N=8 | QAX576 10mg/kg N=8 | Placebo N=6 |
|---|---|---|---|---|---|
| | Days | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD |
| $FEV_1$ (L) | Screening | 2.39 ± 1.51 | 3.53 ± 0.67 | 3.52 ± 0.72 | 2.62 ± 1.13 |
| | Day 1 pre-dose | 2.39 ± 1.27 | 3.41 ± 0.72 | 3.47 ± 0.74 | 2.55 ± 1.25 |
| | Day 2 | 2.59 ± 1.50 | 3.37 ± 0.70 | 3.43 ± 0.77 | 2.58 ± 0.98 |
| | Day 22 pre-dose | 2.17 ± 1.02 | 3.38 ± 0.80 | 3.46 ± 0.76 | 2.62 ± 0.98 |
| | Day 43 pre-dose | 2.15 ± 1.06 | 3.41 ± 0.81 | 3.36 ± 0.72 | 2.64 ± 1.14 |
| | Day 64 | 2.22 ± 1.09 | 3.39 ± 0.70 | 3.34 ± 0.71 | 2.68 ± 1.15 |
| FVC (L) | Screening | 3.50 ± 1.63 | 5.24 ± 0.54 | 4.54 ± 0.84 | 3.92 ± 1.26 |
| | Day 1 pre-dose | 3.56 ± 1.43 | 5.17 ± 0.48 | 4.60 ± 0.87 | 3.82 ± 1.44 |
| | Day 2 | 3.77 ± 1.53 | 5.16 ± 0.43 | 4.62 ± 0.93 | 3.92 ± 1.24 |
| | Day 22 pre-dose | 3.30 ± 1.15 | 5.14 ± 0.57 | 4.51 ± 0.96 | 4.01 ± 1.23 |
| | Day 43 pre-dose | 3.33 ± 1.15 | 5.14 ± 0.54 | 4.33 ± 0.81 | 4.04 ± 1.39 |
| | Day 64 | 3.44 ± 1.14 | 5.14 ± 0.53 | 4.33 ± 0.82 | 4.01 ± 1.47 |
| exNO (ppb) | Day 1 pre-dose | 27.1 ± 13.8 | 43.2 ± 18.7 | 36.8 ± 29.6 | 61.3 ± 54.8 |
| | Day 2 | 24.4 ± 13.3 | 40.6 ± 12.8 | 31.6 ± 21.3 | 67.0 ± 58.4 |
| | Day 22 pre-dose | 23.0 ± 16.0 | 37.1 ± 12.9 | 39.2 ± 34.6 | 69.3 ± 66.0 |
| | Day 43 pre-dose | 20.5 ± 7.8 | 31.0 ± 14.8 | 45.8 ± 31.4 | 66.2 ± 60.6 |
| | Day 64 | 24.4 ± 8.5 | 30.9 ± 14.0 | 35.0 ± 23.8 | 68.8 ± 60.6 |

**Summary of PiKo®-1$FEV_1$ alerts and rescue medication**

| | | QAX576 1mg/kg N=8 | QAX576 3mg/kg N=8 | QAX576 10mg/kg N=8 | Placebo N=6 |
|---|---|---|---|---|---|
| Days 3-21 | Subjects with alerts n(%) | 0 (0%) | 2 (25%) | 3 (37.5%) | 0 (0%) |
| | Total number of alerts N | 0 | 5 | 22 | 0 |
| | Subjects with rescue medication n(%) | 0 (0%) | 4 (50%) | 2 (25%) | 2 (33.3%) |
| Days 23-42 | Subjects with alerts n(%) | 0 (0%) | 1 (12.5%) | 1 (12.5%) | 0 (0%) |
| | Total number of alerts N | 0 | 2 | 7 | 0 |
| | Subjects with rescue medication n(%) | 0 (0%) | 1 (12.5%) | 0 (0%) | 0 (0%) |
| Days 44-63 | Subjects with alerts n(%) | 0 (0%) | 1 (12.5%) | 2 (25%) | 0 (0%) |
| | Total number of alerts N | 0 | 3 | 10 | 1 |
| | Subjects with rescue medication n(%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (16.7%) |
| Days 65-91 | Subjects with alerts n(%) | 0 (0%) | 0 (0%) | 2 (25%) | 1 (16.7%) |
| | Total number of alerts n | 0 | 0 | 8 | 1 |
| | Subjects with rescue medication n(%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

## Safety Results

### Adverse Events by System Organ Class

| | -QAX576- | | | | |
|---|---|---|---|---|---|
| | 1 mg/kg N=8 | 3 mg/kg N=8 | 10 mg/kg N=8 | Placebo N=6 | Total N=30 |
| Body system | n(%) | n(%) | n(%) | n(%) | n(%) |
| Subjects with AE(s) | 1(12.5) | 8(100) | 5(62.5) | 3(50.0) | 17(56.7) |
| System organ class | | | | | |
| Infections and infestations | 0(0.0) | 4(50.0) | 2(25.0) | 2(33.3) | 8(26.7) |
| Respiratory, thoracic and mediastinal disorders | 0(0.0) | 4(50.0) | 1(12.5) | 2(33.3) | 7(23.3) |
| Injury, poisoning and procedural complications | 0(0.0) | 0(0.0) | 3(37.5) | 1(16.7) | 4(13.3) |
| Nervous system disorders | 0(0.0) | 3(37.5) | 0(0.0) | 1(16.7) | 4(13.3) |
| Gastrointestinal disorders | 0(0.0) | 1(12.5) | 1(12.5) | 1(16.7) | 3(10.0) |
| General disorders and administration site conditions | 0(0.0) | 2(25.0) | 0(0.0) | 1(16.7) | 3(10.0) |
| Musculoskeletal and connective tissue disorders | 0(0.0) | 1(12.5) | 0(0.0) | 1(16.7) | 2(6.7) |
| Cardiac disorders | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Eye disorders | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Investigations | 1(12.5) | 0(0.0) | 0(0.0) | 0(0.0) | 1(3.3) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 1(12.5) | 0(0.0) | 0(0.0) | 0(0.0) | 1(3.3) |
| Skin and subcutaneous tissue disorders | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |

## 10 Most Frequently Reported AEs Overall by Preferred Term n (%)

| | 1 mg/kg N=8 n(%) | 3 mg/kg N=8 n(%) | 10 mg/kg N=8 n(%) | Placebo N=6 n(%) | Total N=30 n (%) |
|---|---|---|---|---|---|
| Subjects with AE(s) | 1(12.5) | 8(100) | 5(62.5) | 3(50.0) | 17(56.7) |
| Preferred term | | | | | |
| Nasopharyngitis | 0(0.0) | 3(37.5) | 1(12.5) | 1(16.7) | 5(16.7) |
| Headache | 0(0.0) | 2(25.0) | 0(0.0) | 1(16.7) | 3(10.0) |
| Chest discomfort | 0(0.0) | 1(12.5) | 0(0.0) | 1(16.7) | 2(6.7) |
| Oropharyngeal pain | 0(0.0) | 1(12.5) | 1(12.5) | 0(0.0) | 2(6.7) |
| Rhinorrhoea | 0(0.0) | 1(12.5) | 1(12.5) | 0(0.0) | 2(6.7) |
| Sneezing | 0(0.0) | 1(12.5) | 1(12.5) | 0(0.0) | 2(6.7) |
| Arthralgia | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Blood immunoglobulin E increased | 1(12.5) | 0(0.0) | 0(0.0) | 0(0.0) | 1(3.3) |
| Conjunctivitis | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Cough | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Dermatitis contact | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Diarrhoea | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Dizziness | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Epistaxis | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Furuncle | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Haemangioma of liver | 1(12.5) | 0(0.0) | 0(0.0) | 0(0.0) | 1(3.3) |
| Infusion site swelling | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Lower respiratory tract infection | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Muscle injury | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Myalgia | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Overdose | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Pharyngitis | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Post procedural infection | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Post-traumatic pain | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Procedural pain | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Productive cough | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Supraventricular extrasystoles | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Toothache | 0(0.0) | 1(12.5) | 0(0.0) | 0(0.0) | 1(3.3) |
| Vomiting | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |
| Wheezing | 0(0.0) | 0(0.0) | 0(0.0) | 1(16.7) | 1(3.3) |
| Wrist fracture | 0(0.0) | 0(0.0) | 1(12.5) | 0(0.0) | 1(3.3) |

## Serious Adverse Events and Deaths

| | Novartis product |
|---|---|
| No. (%) of subjects studied | 30 |
| No. (%) of subjects with AE(s) | 17 (56.7) |
| **Number (%) of subjects with serious or other significant events** | n (%) |
| Death | 0 (0.0) |
| SAE(s) | 2 (6.7) |
| Discontinued due to SAE(s) | 2 (6.6) |

1 severe hyperimmunoglobulinemia. 1 paracetamol overdose.

## Other Relevant Findings

None

## Date of Clinical Trial Report

**Definition:** 26 March 2012

## Date Inclusion on Novartis Clinical Trial Results Database

28 March 2012

## Date of Latest Update

28 March 2012