



Clinical trial results:

Double-Blind, Randomized, 8-Week Placebo-Controlled, and 16-Week Open Label Extension Study Investigating the Safety, Pharmacokinetics and Pharmacodynamics of SAR100842 Given Orally to Patients with Diffuse Cutaneous Systemic Sclerosis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-001369-34 |
| Trial protocol | GB DE IT |
| Global end of trial date | 02 April 2014 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 27 April 2016 |
| First version publication date | 28 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | ACT12339 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01651143 |
| WHO universal trial number (UTN) | U1111-1127-2854 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi aventis recherche & développement |
| Sponsor organisation address | 1 avenue Pierre, Brossolette, Chilly-Mazarin, France, 91380 |
| Public contact | Trial Transparency Team, Sanofi-aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi-aventis recherche & développement, Contact-US@sanofi.com |

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 | 28 May 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 02 April 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate safety and tolerability of 8-week oral administration of SAR100842 in subjects with diffuse cutaneous systemic sclerosis/scleroderma (dcSSc).

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 04 January 2013 |
| 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 | France: 6 |
| Country: Number of subjects enrolled | United Kingdom: 5 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Switzerland: 4 |
| Country: Number of subjects enrolled | United States: 16 |
| Worldwide total number of subjects | 32 |
| EEA total number of subjects | 12 |

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 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 29 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 12 sites in 5 countries. A total of 48 subjects were screened between 4 January 2013 and 12 September 2013.

Pre-assignment

Screening details:

Of 48 screened subjects, 16 were screen failure and 32 subjects were randomized and treated.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Core Part |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo-Core Part |

Arm description:

Placebo matched to SAR100842 for 8 weeks.

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo- Core Part |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo matched to SAR100842 300 mg (100 mg +200 mg tablets), given twice daily (2 tablets in the morning and 2 tablets in the evening) for a total daily dose of 600 mg for 8 weeks.

| | |
|------------------|---------------------|
| Arm title | SAR100842-Core Part |
|------------------|---------------------|

Arm description:

SAR100842 300 mg BID for 8 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | SAR100842 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

SAR100842 300 mg (100 mg + 200 mg tablets), given twice daily (2 tablets in the morning and 2 tablets in the evening) for a total daily dose of 600 mg for 8 weeks.

| Number of subjects in period 1 | Placebo-Core Part | SAR100842-Core Part |
|---------------------------------------|-------------------|---------------------|
| Started | 17 | 15 |
| Completed | 17 | 14 |
| Not completed | 0 | 1 |
| Personal request | - | 1 |

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Extension Part |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo/SAR100842-Extension Part |

Arm description:

Subjects who received placebo in core part were treated with SAR100842 for further 16 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | SAR100842 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

SAR100842 300 mg (100 mg + 200 mg tablets), given twice daily (2 tablets in the morning and 2 tablets in the evening) for a total daily dose of 600 mg for 16 weeks.

| | |
|------------------|--------------------------|
| Arm title | SAR100842-Extension Part |
|------------------|--------------------------|

Arm description:

Subjects who received SAR100842 in core part were treated with SAR100842 for further 16 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | SAR100842 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

SAR100842 300 mg (100 mg + 200 mg tablets), given twice daily (2 tablets in the morning and 2 tablets in the evening) for a total daily dose of 600 mg for 16 weeks.

| Number of subjects in period 2^[1] | Placebo/SAR100842-Extension Part | SAR100842-Extension Part |
|---|----------------------------------|--------------------------|
| Started | 16 | 14 |
| Completed | 15 | 13 |
| Not completed | 1 | 1 |
| Adverse event | 1 | 1 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One subject from placebo core part group did not continue in Extension part.

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Placebo-Core Part |
|-----------------------|-------------------|

Reporting group description:

Placebo matched to SAR100842 for 8 weeks.

| | |
|-----------------------|---------------------|
| Reporting group title | SAR100842-Core Part |
|-----------------------|---------------------|

Reporting group description:

SAR100842 300 mg BID for 8 weeks.

| Reporting group values | Placebo-Core Part | SAR100842-Core Part | Total |
|------------------------------------|-------------------|---------------------|-------|
| Number of subjects | 17 | 15 | 32 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|----|
| Age continuous Units: years arithmetic mean standard deviation | 50.6 ± 11.3 | 48.8 ± 10.3 | - |
| Gender categorical Units: Subjects | | | |
| Female | 12 | 9 | 21 |
| Male | 5 | 6 | 11 |

End points

End points reporting groups

| | |
|--|----------------------------------|
| Reporting group title | Placebo-Core Part |
| Reporting group description: Placebo matched to SAR100842 for 8 weeks. | |
| Reporting group title | SAR100842-Core Part |
| Reporting group description: SAR100842 300 mg BID for 8 weeks. | |
| Reporting group title | Placebo/SAR100842-Extension Part |
| Reporting group description: Subjects who received placebo in core part were treated with SAR100842 for further 16 weeks. | |
| Reporting group title | SAR100842-Extension Part |
| Reporting group description: Subjects who received SAR100842 in core part were treated with SAR100842 for further 16 weeks. | |

Primary: Treatment Emergent Adverse Event - Safety Population

| | |
|---|---|
| End point title | Treatment Emergent Adverse Event - Safety Population ^[1] |
| End point description: Adverse Event (AE) was defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which did not necessarily have to have a causal relationship with this treatment. Analysis was performed on safety population defined as randomized and treated subjects in the core part (respectively extension part, for extension part analysis), analyzed according to the treatment actually received. | |
| End point type | Primary |
| End point timeframe: Baseline Up to Week 8 - Core part, Week 8 to Week 24 - Extension part | |
| 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: The data reported are qualitative, hence, no statistical analysis is provided. | |

| End point values | Placebo-Core Part | SAR100842-Core Part | Placebo/SAR100842-Extension Part | SAR100842-Extension Part |
|--|-------------------|---------------------|----------------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 16 | 14 |
| Units: subjects | | | | |
| TEAE | 12 | 12 | 13 | 10 |
| Treatment emergent SAE | 0 | 1 | 1 | 1 |
| TEAE leading permanent treatment discontinuation | 0 | 0 | 1 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Modified Rodnan Skin Score (mRSS)

score Up to Week 24: mITT Population

| | |
|-----------------|--|
| End point title | Change From Baseline in Total Modified Rodnan Skin Score (mRSS) score Up to Week 24: mITT Population |
|-----------------|--|

End point description:

mRSS (measurement of skin thickening) was assessed by palpation of the skin in 17 areas of the body using 0 - 3 scale (0 = normal, 1 = mild thickness, 2 = moderate thickness and 3 = severe thickness). Total skin score can range from 0 (no thickening) to 51 (severe thickening in all 17 areas).

Modified intent-to-treat (mITT)

population was defined as randomized and treated subjects with at least 1 post- Investigational medicinal product (IMP)-administration measurement during the core part (respectively extension part, for extension part analysis).

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

End point timeframe:

Baseline, Week 8 - Core part, Week 8 to Week 24 - Extension part

| End point values | Placebo-Core Part | SAR100842-Core Part | Placebo/SAR100842-Extension Part | SAR100842-Extension Part |
|--------------------------------------|---------------------|---------------------|----------------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 13 | 14 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -2.76 (\pm 4.85) | -3.4 (\pm 4.08) | -7.31 (\pm 4.59) | -7.36 (\pm 4.24) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Scleroderma Health Assessment Questionnaire (SHAQ) Total Score Up to Week 24: mITT Population

| | |
|-----------------|---|
| End point title | Change From Baseline in Scleroderma Health Assessment Questionnaire (SHAQ) Total Score Up to Week 24: mITT Population |
|-----------------|---|

End point description:

The SHAQ included a standard Health Assessment Questionnaire Disability Index (HAQ-DI) subscore and 5 visual analog scales (VAS) for severity assessments of Raynaud's phenomenon, breathing, digital ulcers, gastrointestinal disease and overall disease. The HAQ-DI was scored 0 to 3 from no disability to the most severe one. Analysis was performed on mITT population (core part and extension part).

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

End point timeframe:

Baseline, Week 8 - Core part, Week 8 to Week 24 - Extension part

| End point values | Placebo-Core Part | SAR100842-Core Part | Placebo/SAR100842-Extension Part | SAR100842-Extension Part |
|--------------------------------------|-------------------|---------------------|----------------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 15 | 13 | 14 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | 0 (\pm 0.33) | -0.14 (\pm 0.3) | -0.23 (\pm 0.3) | -0.15 (\pm 0.33) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responder Based on 4 Skin Biomarkers At Week 8: PD Population

| | |
|-----------------|---|
| End point title | Percentage of Responder Based on 4 Skin Biomarkers At Week 8: PD Population |
|-----------------|---|

End point description:

A subjects was considered as a responder if at least 20% reduction from baseline was demonstrated in 2 of these 4 biomarkers (cartilage oligomeric matrix protein [COMP], Collagen 1A1 [COL1A1] messenger ribonucleic acid [mRNA], thrombospondin 1 [TSP1] and alpha-smooth muscle actin [α -SMA] positive cells. Pharmacodynamics (PD) population, included randomized and treated subjects who received at least 4 weeks of IMP with at least a baseline and a post-baseline assessment.

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

End point timeframe:

Baseline, Week 8

| End point values | Placebo-Core Part | SAR100842-Core Part | | |
|-------------------------------|-------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 14 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 47.1 | 64.3 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (core & extension part: Week 8, 24) regardless of seriousness or relationship to investigational product. Analysis was performed on safety population.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' [from the first administration of the study drug to the last administration of the study drug during the core/extension part + 5 days (5 half-lives)].

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

Dictionary used

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|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 17.0 |

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Placebo-Core Part |
|-----------------------|-------------------|

Reporting group description:

Placebo matched to SAR100842 for 8 weeks.

| | |
|-----------------------|---------------------|
| Reporting group title | SAR100842-Core Part |
|-----------------------|---------------------|

Reporting group description:

SAR100842 300 mg BID for 8 weeks.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Placebo/SAR100842-Extension Part |
|-----------------------|----------------------------------|

Reporting group description:

Subjects who received placebo in core part were treated with SAR100842 for further 16 weeks.

| | |
|-----------------------|--------------------------|
| Reporting group title | SAR100842-Extension Part |
|-----------------------|--------------------------|

Reporting group description:

Subjects who received SAR100842 in core part were treated with SAR100842 for further 16 weeks.

| Serious adverse events | Placebo-Core Part | SAR100842-Core Part | Placebo/SAR100842-Extension Part |
|---|-------------------|---------------------|----------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 1 / 16 (6.25%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Infected Skin Ulcer | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------------------|--|--|
| Serious adverse events | SAR100842- Extension Part | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Infected Skin Ulcer | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| 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 | Placebo-Core Part | SAR100842-Core Part | Placebo/SAR100842-Extension Part |
|---|-------------------|---------------------|----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 17 (70.59%) | 11 / 15 (73.33%) | 13 / 16 (81.25%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin Papilloma | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hot Flush | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Orthostatic Hypotension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Surgical and medical procedures | | | |
| Sinus Operation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 2 | 0 | 1 |
| Device Leakage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 1 | 0 | 2 |
| Feeling Abnormal | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Non-Cardiac Chest Pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oedema Peripheral | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Ulcer | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Menstruation Irregular | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vaginal Discharge | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vaginal Haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 1 | 0 | 2 |
| Nasal Dryness | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oropharyngeal Pain | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Pleural Effusion subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Pulmonary Mass subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Rales subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Psychiatric disorders Depression subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Investigations Lymphocyte Count Decreased subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Prothrombin Time Prolonged subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Injury, poisoning and procedural complications Accidental Overdose subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Post Procedural Discomfort subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Procedural Pain | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Thermal Burn subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Cardiac disorders Cardiac Failure subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Palpitations subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Nervous system disorders Amnesia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 3 / 15 (20.00%) 3 | 3 / 16 (18.75%) 3 |
| Hyperaesthesia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Migraine subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Muscle Contractions Involuntary subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Paraesthesia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Eye disorders | | | |
| Lacrimation Increased subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Pterygium subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Vitreous Detachment subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal Pain subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Abdominal Pain Upper subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 1 / 15 (6.67%) 1 | 0 / 16 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 2 / 15 (13.33%) 2 | 1 / 16 (6.25%) 1 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 2 / 16 (12.50%) 2 |
| Gastrooesophageal Reflux Disease subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 1 / 15 (6.67%) 1 | 1 / 16 (6.25%) 1 |
| Mouth Ulceration subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Nausea | | | |

| | | | |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 17 (5.88%) | 2 / 15 (13.33%) | 2 / 16 (12.50%) |
| occurrences (all) | 1 | 2 | 2 |
| Oral Pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Tongue Ulceration | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 15 (6.67%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 1 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Keloid Scar | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Night Sweats | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Palmar Erythema | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Photosensitivity Reaction | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus Generalised | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|----------------|----------------|-----------------|
| Skin Depigmentation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin Discolouration | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin Discomfort | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin Induration | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin Lesion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin Ulcer | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 1 | 0 | 2 |
| Swelling Face | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 3 / 16 (18.75%) |
| occurrences (all) | 0 | 0 | 3 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back Pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Limb Discomfort | | | |

| | | | |
|----------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle Spasms | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal Discomfort | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal Stiffness | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pain In Extremity | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Temporomandibular Joint Syndrome | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Application Site Cellulitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis Viral | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Herpes Zoster | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 15 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 15 (6.67%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Urinary Tract Infection subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 15 (0.00%) 0 | 1 / 16 (6.25%) 1 |

| | | | |
|---|--|--|--|
| Non-serious adverse events | SAR100842- Extension Part | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 9 / 14 (64.29%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin Papilloma subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Vascular disorders Flushing subjects affected / exposed occurrences (all) Hot Flush subjects affected / exposed occurrences (all) Hypotension subjects affected / exposed occurrences (all) Orthostatic Hypotension subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 | | |
| Surgical and medical procedures Sinus Operation subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|----------------|--|--|
| Asthenia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Device Leakage | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Feeling Abnormal | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Non-Cardiac Chest Pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema Peripheral | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ulcer | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |
| Menstruation Irregular | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vaginal Discharge | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vaginal Haemorrhage | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|----------------|--|--|
| Cough | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal Dryness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pleural Effusion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pulmonary Mass | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rales | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Lymphocyte Count Decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Prothrombin Time Prolonged | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|---------------------|--|--|
| Accidental Overdose subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Fall subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Post Procedural Discomfort subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Procedural Pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Thermal Burn subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Cardiac disorders Cardiac Failure subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Palpitations subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Nervous system disorders Amnesia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Headache subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | | |
| Hyperaesthesia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Migraine | | | |

| | | | |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Muscle Contractions Involuntary | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Lacrimation Increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pterygium | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vitreous Detachment | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspepsia | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal Reflux Disease | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Mouth Ulceration | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral Pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tongue Ulceration | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Keloid Scar | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Night Sweats | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Palmar Erythema | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|---------------------|--|--|
| Photosensitivity Reaction subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Pruritus Generalised subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Skin Depigmentation subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Skin Discolouration subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Skin Discomfort subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Skin Induration subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Skin Lesion subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Skin Ulcer subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Swelling Face subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|----------------------------------|----------------|--|--|
| Arthralgia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Back Pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Limb Discomfort | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle Spasms | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal Discomfort | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal Stiffness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain In Extremity | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Temporomandibular Joint Syndrome | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Application Site Cellulitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis Viral | | | |

| | | | |
|------------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes Zoster | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | | |
| occurrences (all) | 2 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 19 February 2013 | <p>A 16 week extension was proposed to all subjects willing to continue on SAR100842, after they had completed the 8 week treatment and procedures. This longer exposure would provide additional long term safety data, and additional guidance for the selection and monitoring of subjects in longer further studies. Since SAR100842 was to be given in open label, subjects initially treated with placebo had the opportunity to receive the drug.</p> <p>The following sections was updated: A summary of the 6-month toxicology data supporting this extension was added, and the rationale of this extension was provided. A secondary objective and endpoint on safety and tolerability during the extension part was added. The inclusion/exclusion criteria for the extension were described. Only subjects who had completed the treatment and all procedures of the core part were included. All events described as reason for discontinuation in the core part were listed as exclusion criteria of the extension part, details of the volume of blood samples for the extension were provided (50ml to 65 ml depending on the number of blood samples taken). Clinical and laboratory safety were to be assessed through vital signs, physical examination, blood and urine samples. Depending on the duration of the window, additional physical examination, body weight and blood samples were to be performed at inclusion in the extension part. An optional skin biopsy was to be proposed at the end of the open label extension. Two informed consents were added, one for the extension part and another for the skin biopsy at the end of open label treatment, subjects who stopped the study treatment prematurely had the procedures listed in the end of treatment visit except that the last IMP was not to be given. Any procedure related to this intake such as PK sampling, and blood pressure measurement 4 hours after the intake, was not applicable. Mycophenolate mofetil greater than 2gm a day was added in exclusion criteria.</p> |
| 03 December 2013 | <p>One of the secondary objective of this study was to explore the effect of SAR100842 in subjects with diffuse cutaneous systemic sclerosis/scleroderma (dcSSc) as measured by disease related biomarkers.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported