



Clinical trial results:

A Multicenter Single-Arm Open Label Extension Study Evaluating The Long Term Safety And Tolerability Of SAR339658 In Patients With Ulcerative Colitis (UC)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-001012-30 |
| Trial protocol | IT AT BE PL DE |
| Global end of trial date | 25 April 2016 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 05 January 2017 |
| First version publication date | 05 January 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | LTS12593 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01861249 |
| WHO universal trial number (UTN) | U1111-1141-4634 |

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 & Developpement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi Aventis Recherche & Developpement, 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 | 05 May 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 25 April 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and tolerability of SAR339658.

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 | 23 July 2013 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 24 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | United States: 6 |
| Worldwide total number of subjects | 6 |
| 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) | 0 |

| | |
|----------------------|---|
| Adults (18-64 years) | 6 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects who completed the 8-week treatment in the ACT12688 study (EudraCT no. 2012-002013-19) were offered the option to participate in this long-term study. 6/17 subjects consented in participating in the study prior to the decision to discontinue both studies because of slow enrollment.

Pre-assignment

Screening details:

The screening visit was the Week 8 visit of the ACT12688 study. All subjects who consented received SAR339658 with dose regimen adjusted according to the clinical response at Week 8 of the ACT12688 study.

Period 1

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

Arms

| | |
|-----------|-----------|
| Arm title | SAR339658 |
|-----------|-----------|

Arm description:

SAR339658 20 mg/kg infusion every 4 weeks (q4w) from Week 2 (if clinical response at Week 8 in ACT12688 trial) or every 2 weeks (q2w) at Weeks 0, 2, 4 and 6 and then q4w (if no clinical response at week 8 in ACT12688 trial) for a total of 62 weeks.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Vatelizumab |
| Investigational medicinal product code | SAR339658 |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

SAR339658 20 mg/kg infusion over 60 minutes (for subjects weighing <120 kg) or 120 minutes (for subjects weighing >120 kg).

| Number of subjects in period 1 | SAR339658 |
|--------------------------------|-----------|
| Started | 6 |
| Treated | 6 |
| Completed | 0 |
| Not completed | 6 |
| Sponsor's decision | 3 |
| Lack of efficacy | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | SAR339658 |
|-----------------------|-----------|

Reporting group description:

SAR339658 20 mg/kg infusion every 4 weeks (q4w) from Week 2 (if clinical response at Week 8 in ACT12688 trial) or every 2 weeks (q2w) at Weeks 0, 2, 4 and 6 and then q4w (if no clinical response at week 8 in ACT12688 trial) for a total of 62 weeks.

| Reporting group values | SAR339658 | Total | |
|---|-----------|-------|--|
| Number of subjects | 6 | 6 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 6 | 6 | |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 3 | |
| Male | 3 | 3 | |
| Product received in the ACT12688 study Units: Subjects | | | |
| Placebo | 2 | 2 | |
| SAR339658 | 4 | 4 | |
| Clinical Response at Week 8 of ACT12688 Units: Subjects | | | |
| Yes | 1 | 1 | |
| No | 5 | 5 | |

End points

End points reporting groups

| | |
|--|--------------------------------------|
| Reporting group title | SAR339658 |
| Reporting group description: SAR339658 20 mg/kg infusion every 4 weeks (q4w) from Week 2 (if clinical response at Week 8 in ACT12688 trial) or every 2 weeks (q2w) at Weeks 0, 2, 4 and 6 and then q4w (if no clinical response at week 8 in ACT12688 trial) for a total of 62 weeks. | |
| Subject analysis set title | SAR339658 - Post-Treatment Follow-up |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects who received at least one dose of SAR339658 and consented in participating in the post-treatment long term safety follow-up. | |

Primary: Number of Subjects Who Experienced Adverse Events

| | |
|---|--|
| End point title | Number of Subjects Who Experienced Adverse Events ^[1] |
| End point description: Reported adverse events (AEs) were classified according to seriousness and outcome. Analysis was performed on the safety population that included all subjects who received at least 1 dose of the product in this extension study. | |
| End point type | Primary |
| End point timeframe: From enrollment in the study up to the last visit in the study (17 weeks max instead of 69 as planned) | |
| 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 endpoint is descriptive in nature. | |

| | | | | |
|--|-----------------|--|--|--|
| End point values | SAR339658 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: subjects | | | | |
| Any AEs | 5 | | | |
| - Serious AEs | 0 | | | |
| - AEs leading to treatment discontinuation | 0 | | | |
| - AEs leading to death | 0 | | | |
| AEs after 1st dose in the study | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Abnormality in Laboratory Tests and/or Vital Signs

| | |
|--|---|
| End point title | Number of Subjects with Clinically Significant Abnormality in Laboratory Tests and/or Vital Signs |
| End point description: Laboratory tests included hematology; liver function test; lipids profile; renal function test; electrolytes and urine analysis. Vital signs included temperature; blood pressure; heart rate and respiration rate. Analysis was performed on safety population. | |

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From enrollment in the study up to the last visit in the study (17 weeks max instead of 69 as planned). | |

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | SAR339658 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: subjects | | | | |
| Laboratory tests | 0 | | | |
| Vital signs | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Remission (Per Mayo Score) at Week 62

| | |
|-----------------|--|
| End point title | Percentage of Subjects with Clinical Remission (Per Mayo Score) at Week 62 |
|-----------------|--|

End point description:

Clinical remission per Mayo score was defined as a total Mayo score of 2 points or lower, with no individual sub score exceeding 1 point, and with the endoscopic sub-score read by a central reader.

The Mayo Score is a discrete ordinal scale to assess ulcerative colitis activity. It is a composite of 4 sub-scores for stool frequency, rectal bleeding, endoscopy, and Physician's Global Assessment (PGAS), each of which ranges from 0 (normal) to 3 (severe disease). Total score ranges from 0 (normal or inactive disease) to 12 (severe disease).

Analysis was not performed because of the small number of subjects.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 62 | |

| | | | | |
|-------------------------------|------------------|--|--|--|
| End point values | SAR339658 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

Notes:

[2] - Endpoint was not analyzed because of the small number of subjects and the shorter follow-up

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Mucosal Healing (Per Mayo Score) at Week 62

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Mucosal Healing (Per Mayo Score) at Week 62 |
|-----------------|---|

End point description:

Mucosal healing was defined as a Mayo endoscopy sub-score of 0 or 1, obtained from colonoscopy (read by a central reader). Possible sub-scores were as follows: 0 = Normal or inactive disease, 1 = Mild disease (erythema, decreased vascular pattern, and mild friability), 2 = Moderate disease (marked erythema, absent vascular pattern, friability, and erosions), 3 = Severe disease (spontaneous bleeding, ulceration).

Analysis was not performed because of the small number of subjects.

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

End point timeframe:

Baseline to Week 62

| | | | | |
|-------------------------------|------------------|--|--|--|
| End point values | SAR339658 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[3] | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

Notes:

[3] - Endpoint was not analyzed because of the small number of subjects and the shorter follow-up.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Partial Mayo Score at Week 10, 22, 34, 46 and 58

| | |
|-----------------|--|
| End point title | Change From Baseline in the Partial Mayo Score at Week 10, 22, 34, 46 and 58 |
|-----------------|--|

End point description:

Partial Mayo score is calculated as a sum of three sub-scores for stool frequency, rectal bleeding and PGAS. It is in a range from 0-9 points; higher partial Mayo scores indicate more severe disease.

Analysis was not performed because of the small number of subjects.

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

End point timeframe:

Baseline, Week 10, 22, 34, 46 and 58

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | SAR339658 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[4] | | | |
| Units: Units on scale | | | | |
| number (not applicable) | | | | |

Notes:

[4] - Endpoint was not analyzed because of the small number of subjects and the shorter follow-up.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Week 34 and 62

| | |
|-----------------|---|
| End point title | Change From Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) Total Score at Week 34 and 62 |
|-----------------|---|

End point description:

The IBDQ is a self-administered 32-item questionnaire that evaluates the disease specific quality of life across 4 dimensional scores: Bowel, Systemic, Social and Emotional. The total IBDQ score is the sum of the responses to the individual questions and can range from 32 to 224; higher scores indicating a better quality of life.

Analysis was not performed because of the small number of subjects.

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

End point timeframe:

Baseline, Week 34, Week 62

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | SAR339658 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[5] | | | |
| Units: Units on scale | | | | |
| number (not applicable) | | | | |

Notes:

[5] - Endpoint was not analyzed because of the small number of subjects and the shorter follow-up.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Long Term Safety Follow-up: Number of subjects opportunistic or Progressive Multifocal Leukoencephalopathy (PML)

| | |
|-----------------|--|
| End point title | Long Term Safety Follow-up: Number of subjects opportunistic or Progressive Multifocal Leukoencephalopathy (PML) |
|-----------------|--|

End point description:

Subjects were contacted by phone at 3, 6, 12, 18 and 24 months post-treatment. During the phone contact, subject was asked specific questions regarding any new signs or symptoms indicative of infection. Any positive findings on questioning were expeditiously referred to a physician for additional evaluation. If any abnormal signs and symptoms are observed or identified, the subject was subsequently referred to an infectious disease specialist or a neurologist for a complete assessment.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Up to 24 months after the last dose of investigational medicinal product (IMP) [long-term safety follow-up]

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | SAR339658 - Post-Treatment Follow-up | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: subjects | 0 | | | |

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 (17 weeks max) regardless of seriousness or relationship to study drug.

Adverse event reporting additional description:

Reported AEs and deaths are treatment-emergent that is AEs that developed/worsened and deaths that occurred during the 'on treatment period' (from the first dose in the study up to the last visit in the study).

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

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

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|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

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|-----------------------|-----------|
| Reporting group title | SAR339658 |
|-----------------------|-----------|

Reporting group description:

Subjects with clinical response at Week 8 in study ACT12688 received SAR339658 20 mg/kg q4w.

Subjects with no clinical response at week 8 in study ACT12688 received SAR339658 20 mg/kg q2w for eight weeks followed by q4w.

| Serious adverse events | SAR339658 | | |
|---|---------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | SAR339658 | | |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | | |
| Injury, poisoning and procedural complications | | | |
| Accidental Overdose | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | | |
| occurrences (all) | 1 | | |
| Congenital, familial and genetic disorders | | | |
| Atrial Septal Defect | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|---------------------|--|--|
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |
| Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |
| Gastrointestinal disorders Dental Caries subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |
| Skin and subcutaneous tissue disorders Night Sweats subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |
| Infections and infestations Herpes Zoster subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

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|--|
| The number of subjects enrolled was much smaller than planned (6 instead of 80) because of early termination due to slow enrollment. |
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Notes: