



## Clinical trial results:

### An Open Label Non-Randomized Phase 2 Study Evaluating SAR3419, an Anti-CD19 Antibody – Maytansine Conjugate, Administered as Single Agent by Intravenous Infusion to Patients With Relapsed or Refractory CD19+ Diffuse Large B Cell Lymphoma

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2011-003657-26  |
| Trial protocol           | CZ BE ES IT GB  |
| Global end of trial date | 10 October 2016 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 14 October 2017 |
| First version publication date | 14 October 2017 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | ARD10248 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |                      |
|------------------------------------|----------------------|
| ISRCTN number                      | -                    |
| ClinicalTrials.gov id (NCT number) | NCT01472887          |
| WHO universal trial number (UTN)   | U1111-1115-3349      |
| Other trial identifiers            | Study Name: STARLYTE |

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                       | 25 October 2016 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 10 October 2016 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To determine the objective response rate (ORR) produced by SAR3419 in subjects with CD19+ diffuse large B-cell lymphoma (DLBCL) after failure of at least 1 prior line of standard therapy.

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                          | 19 January 2012 |
| 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 | Poland: 4          |
| Country: Number of subjects enrolled | Spain: 10          |
| Country: Number of subjects enrolled | United Kingdom: 7  |
| Country: Number of subjects enrolled | Belgium: 5         |
| Country: Number of subjects enrolled | Czech Republic: 10 |
| Country: Number of subjects enrolled | Italy: 12          |
| Country: Number of subjects enrolled | Israel: 5          |
| Country: Number of subjects enrolled | Turkey: 2          |
| Country: Number of subjects enrolled | United States: 6   |
| Worldwide total number of subjects   | 61                 |
| EEA total number of subjects         | 48                 |

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)                      | 17 |
| From 65 to 84 years                       | 42 |
| 85 years and over                         | 2  |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 28 sites in 9 countries between 19 January 2012 and 10 October 2016. A total of 79 subjects were screened in the study, out of which 18 were screen failures and 61 were enrolled and treated in the study.

### Pre-assignment

Screening details:

Subjects enrolled in the study to evaluate the efficacy and safety of SAR3419 in adult subjects with CD19+ DLBCL with relapsed or refractory disease after failure of at least 1 prior line of standard therapy.

### Period 1

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

### Arms

|           |         |
|-----------|---------|
| Arm title | SAR3419 |
|-----------|---------|

Arm description:

SAR3419 55 mg/m<sup>2</sup> once weekly for 4 weeks, followed by 1 week rest, and thereafter, every 2 weeks until disease progression (DP), unacceptable toxicity, or any other reason for treatment discontinuation.

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | SAR3419                               |
| Investigational medicinal product code |                                       |
| Other name                             | Coltuximab ravtansine                 |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

SAR3419 administered at initial infusion rate of 1 mL/min for 30 minutes and then increased progressively by 0.5 mL/min increments at 15-minute intervals up to 3 mL/min.

| Number of subjects in period 1 | SAR3419 |
|--------------------------------|---------|
| Started                        | 61      |
| Completed                      | 0       |
| Not completed                  | 61      |
| Disease progression            | 49      |
| Adverse event                  | 9       |
| Other than specified           | 3       |

## Baseline characteristics

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### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | SAR3419 |
|-----------------------|---------|

Reporting group description:

SAR3419 55 mg/m<sup>2</sup> once weekly for 4 weeks, followed by 1 week rest, and thereafter, every 2 weeks until disease progression (DP), unacceptable toxicity, or any other reason for treatment discontinuation.

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| Reporting group values                                                  | SAR3419        | Total |  |
|-------------------------------------------------------------------------|----------------|-------|--|
| Number of subjects                                                      | 61             | 61    |  |
| Age categorical<br>Units: Subjects                                      |                |       |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 68.1<br>± 11.3 | -     |  |
| Gender categorical<br>Units: Subjects                                   |                |       |  |
| Female                                                                  | 30             | 30    |  |
| Male                                                                    | 31             | 31    |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                        |         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Reporting group title                                                                                                                                                                                                                                  | SAR3419 |
| Reporting group description:<br>SAR3419 55 mg/m <sup>2</sup> once weekly for 4 weeks, followed by 1 week rest, and thereafter, every 2 weeks until disease progression (DP), unacceptable toxicity, or any other reason for treatment discontinuation. |         |

### Primary: Percentage of Subjects with Objective Response (OR)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Percentage of Subjects with Objective Response (OR) <sup>[1]</sup> |
| End point description:<br>OR reported as percentage of subjects achieving complete response (CR) or partial response (PR) relative to total number of subjects in per protocol (PP) population. As per Revised Response Criteria for Malignant Lymphoma, CR:Disappearance of all evidence of disease (nodal masses: [18F] Fluorodeoxyglucose[FDG]-avid or Positron emission tomography[PET] positive before therapy;Variably FDG-avid or if PET negative,regression to normal size; spleen/liver: not palpable,nodules disappeared; bone marrow infiltration cleared on repeat biopsy or negative immunohistochemistry) and PR: Regression of measurable disease, no new sites (≥50% decrease in sum of product of diameters of up to 6 largest dominant nodes or masses; no increase in size of other nodes, liver or spleen). PP population: all subjects who received at least 1 dose of study drug with no protocol deviation impacting efficacy at study entry & had an evaluable response assessment during treatment period or at end of treatment (EOT). |                                                                    |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Primary                                                            |
| End point timeframe:<br>Baseline, every 12 weeks up to DP, or any other reason for treatment discontinuation (upto 95.14 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

| End point values                 | SAR3419             |  |  |  |
|----------------------------------|---------------------|--|--|--|
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 41                  |  |  |  |
| Units: percentage of subjects    |                     |  |  |  |
| number (confidence interval 90%) | 43.9 (30.6 to 57.9) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of response (DOR)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Duration of response (DOR) |
| End point description:<br>Duration of tumor response was defined as the time interval from the date of the first occurrence of CR or PR to the date of the first documentation of disease progression or death due to any reason, whichever occurred first. In the absence of DP or death or further anticancer therapy at the time of the data cut-off date, duration of response was censored to the earliest date of the last evaluable response assessment without evidence of progression and data cut-off date. Analysis was performed on PP |                            |

population using Kaplan-Meier method.

|                                                                                                                    |           |
|--------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                     | Secondary |
| End point timeframe:                                                                                               |           |
| Baseline, every 12 weeks up to DP, or any other reason for treatment discontinuation (maximum duration: 166 weeks) |           |

|                               |                 |  |  |  |
|-------------------------------|-----------------|--|--|--|
| <b>End point values</b>       | SAR3419         |  |  |  |
| Subject group type            | Reporting group |  |  |  |
| Number of subjects analysed   | 41              |  |  |  |
| Units: months                 |                 |  |  |  |
| median (full range (min-max)) | 4.6 (0 to 40)   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression-Free Survival (PFS)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Progression-Free Survival (PFS) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                 |
| Progression-free survival was defined as the time interval from the date of the first study treatment infusion to the date of the first occurrence of progression or death (from any reason), whichever occurred first. In the absence of DP, death or further anticancer therapy at the time of the data cut-off date, the PFS was censored to the earliest date between the date of last evaluable response assessment without evidence of progression and the time of the data cut-off date. Analysis was performed on PP population using Kaplan-Meier method. |                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Secondary                       |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                 |
| Baseline, every 12 weeks up to DP, or any other reason for treatment discontinuation (maximum duration: 166 weeks)                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                 |

|                                  |                    |  |  |  |
|----------------------------------|--------------------|--|--|--|
| <b>End point values</b>          | SAR3419            |  |  |  |
| Subject group type               | Reporting group    |  |  |  |
| Number of subjects analysed      | 41                 |  |  |  |
| Units: months                    |                    |  |  |  |
| median (confidence interval 90%) | 4.4 (3.02 to 5.95) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival (OS)

|                 |                       |
|-----------------|-----------------------|
| End point title | Overall survival (OS) |
|-----------------|-----------------------|

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**End point description:**

Overall survival was defined as the time interval from the date of the first study treatment infusion to the date of death (due to any reason). Analysis was performed using Kaplan-Meier method. Analysis was performed on safety population that included all-treated population who received at least 1 dose of study treatment.

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

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**End point timeframe:**

Baseline, every 12 weeks up to death or study cut-off, whichever came first (maximum duration: 166 weeks)

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|                                  |                     |  |  |  |
|----------------------------------|---------------------|--|--|--|
| <b>End point values</b>          | SAR3419             |  |  |  |
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 61                  |  |  |  |
| Units: months                    |                     |  |  |  |
| median (confidence interval 90%) | 9.2 (6.57 to 12.22) |  |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (maximum duration: 166 weeks) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs and deaths are treatment emergent that is AEs that developed/worsened and deaths that occurred during 'on treatment period' (time from first study treatment infusion to last study treatment infusion + 42 days). Analysis was performed on safety population.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | SAR3419 |
|-----------------------|---------|

Reporting group description:

SAR3419 55 mg/m<sup>2</sup> once weekly for 4 weeks, followed by 1 week rest, and thereafter, every 2 weeks until DP, unacceptable toxicity, or any other reason for treatment discontinuation.

| Serious adverse events                                              | SAR3419          |  |  |
|---------------------------------------------------------------------|------------------|--|--|
| Total subjects affected by serious adverse events                   |                  |  |  |
| subjects affected / exposed                                         | 27 / 61 (44.26%) |  |  |
| number of deaths (all causes)                                       | 7                |  |  |
| number of deaths resulting from adverse events                      |                  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |  |  |
| Gastrointestinal Stromal Tumour                                     |                  |  |  |
| subjects affected / exposed                                         | 1 / 61 (1.64%)   |  |  |
| occurrences causally related to treatment / all                     | 1 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| General disorders and administration site conditions                |                  |  |  |
| Disease Progression                                                 |                  |  |  |
| subjects affected / exposed                                         | 7 / 61 (11.48%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 7            |  |  |
| deaths causally related to treatment / all                          | 0 / 5            |  |  |
| Pyrexia                                                             |                  |  |  |
| subjects affected / exposed                                         | 1 / 61 (1.64%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Acute Pulmonary Oedema                          |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Dyspnoea                                        |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Humerus Fracture                                |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Post Procedural Haematoma                       |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Sinus Bradycardia                               |                |  |  |
| subjects affected / exposed                     | 2 / 61 (3.28%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Spinal Cord Compression                         |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Loss Of Consciousness                           |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| Febrile Neutropenia                             |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 2 / 61 (3.28%) |  |  |
| occurrences causally related to treatment / all | 1 / 5          |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |
| <b>Gastrointestinal disorders</b>               |                |  |  |
| Abdominal Pain                                  |                |  |  |
| subjects affected / exposed                     | 2 / 61 (3.28%) |  |  |
| occurrences causally related to treatment / all | 1 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal Haemorrhage                    |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nausea                                          |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pancreatitis Acute                              |                |  |  |
| subjects affected / exposed                     | 2 / 61 (3.28%) |  |  |
| occurrences causally related to treatment / all | 1 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Hepatobiliary disorders</b>                  |                |  |  |
| Acute Hepatic Failure                           |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Hepatotoxicity                                  |                |  |  |
| subjects affected / exposed                     | 2 / 61 (3.28%) |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Renal and urinary disorders</b>              |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Acute Kidney Injury                             |                |  |  |
| subjects affected / exposed                     | 2 / 61 (3.28%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Renal Failure                                   |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Back Pain                                       |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Intervertebral Disc Protrusion                  |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Herpes Zoster                                   |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumonia                                       |                |  |  |
| subjects affected / exposed                     | 3 / 61 (4.92%) |  |  |
| occurrences causally related to treatment / all | 1 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary Tract Infection                         |                |  |  |
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Hypoglycaemia                                   |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 61 (1.64%) |  |  |
| 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 %

|                                                       |                  |  |  |
|-------------------------------------------------------|------------------|--|--|
| <b>Non-serious adverse events</b>                     | SAR3419          |  |  |
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 50 / 61 (81.97%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Fall                                                  |                  |  |  |
| subjects affected / exposed                           | 6 / 61 (9.84%)   |  |  |
| occurrences (all)                                     | 6                |  |  |
| Vascular disorders                                    |                  |  |  |
| Hypertension                                          |                  |  |  |
| subjects affected / exposed                           | 4 / 61 (6.56%)   |  |  |
| occurrences (all)                                     | 8                |  |  |
| Blood and lymphatic system disorders                  |                  |  |  |
| Thrombocytopenia                                      |                  |  |  |
| subjects affected / exposed                           | 4 / 61 (6.56%)   |  |  |
| occurrences (all)                                     | 6                |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Asthenia                                              |                  |  |  |
| subjects affected / exposed                           | 7 / 61 (11.48%)  |  |  |
| occurrences (all)                                     | 7                |  |  |
| Fatigue                                               |                  |  |  |
| subjects affected / exposed                           | 11 / 61 (18.03%) |  |  |
| occurrences (all)                                     | 13               |  |  |
| Oedema Peripheral                                     |                  |  |  |
| subjects affected / exposed                           | 6 / 61 (9.84%)   |  |  |
| occurrences (all)                                     | 6                |  |  |
| Pyrexia                                               |                  |  |  |
| subjects affected / exposed                           | 4 / 61 (6.56%)   |  |  |
| occurrences (all)                                     | 7                |  |  |
| Gastrointestinal disorders                            |                  |  |  |

|                                                                                                                   |                        |  |  |
|-------------------------------------------------------------------------------------------------------------------|------------------------|--|--|
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)                                                | 5 / 61 (8.20%)<br>6    |  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                                                  | 6 / 61 (9.84%)<br>8    |  |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                                     | 11 / 61 (18.03%)<br>16 |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                                        | 13 / 61 (21.31%)<br>18 |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                                      | 8 / 61 (13.11%)<br>13  |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)      | 12 / 61 (19.67%)<br>13 |  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                                      | 6 / 61 (9.84%)<br>6    |  |  |
| Oropharyngeal Pain<br>subjects affected / exposed<br>occurrences (all)                                            | 4 / 61 (6.56%)<br>4    |  |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                             | 4 / 61 (6.56%)<br>4    |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 5 / 61 (8.20%)<br>7    |  |  |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)                                                     | 7 / 61 (11.48%)<br>7   |  |  |

|                                                                                                              |                      |  |  |
|--------------------------------------------------------------------------------------------------------------|----------------------|--|--|
| Pain In Extremity<br>subjects affected / exposed<br>occurrences (all)                                        | 4 / 61 (6.56%)<br>4  |  |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)           | 4 / 61 (6.56%)<br>6  |  |  |
| Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all)                        | 4 / 61 (6.56%)<br>4  |  |  |
| Metabolism and nutrition disorders<br>Decreased Appetite<br>subjects affected / exposed<br>occurrences (all) | 8 / 61 (13.11%)<br>8 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 30 March 2012    | Following amendments were made: <ul style="list-style-type: none"><li>• Changed the schedule for tumor assessment;</li><li>• Corrected the schedule for tumor assessment along the treatment period mixing response criteria Cheson 1999 and Cheson 2007 applying to Diffuse large B-cell lymphoma (DLBCL) being a FDG-avid, aggressive lymphoma;</li><li>• Changed to the biomarkers analysis;</li><li>• Changed the inclusion/exclusion criteria;</li><li>• Provided the study name as STARLYTE;</li><li>• Clarified the stopping rules and timing of the interim analysis;</li><li>• Changed the investigational medicinal product administration: Corrected the formulation and instruction for preparing and administering the IMP;</li><li>• Updated the safety follow-up period as a 42-day period;</li><li>• Corrected minor inconsistencies/tipos throughout the protocol.</li></ul> |
| 25 May 2012      | <ul style="list-style-type: none"><li>• Changes in inclusion/exclusion criteria;</li><li>• Changed the primary objective as: to evaluate the objective response rate (ORR) of SAR3419 in subjects with CD19+ DLBCL after failure of at least one prior line of standard therapy;</li><li>• Changed the study design as: This is an open label, uncontrolled Phase 2 evaluation of the efficacy and safety of SAR3419 as single agent in subjects with CD19+DLBCL after failure of at least one prior line of standard therapy,</li><li>• Updated the study rationale.</li></ul>                                                                                                                                                                                                                                                                                                               |
| 12 November 2012 | <ul style="list-style-type: none"><li>• Replaced 1 working day with within 24 hours in SAE reporting timelines,</li><li>• Changed minor inconsistencies/tipos throughout the protocol.</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 19 July 2013     | <ul style="list-style-type: none"><li>• Changed the concomitant medication with study treatment;</li><li>• Changed the IP preparation;</li><li>• Clarification on related AE/SAEs occurring during FU period or ongoing at the EOT visit.</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 22 January 2014  | Updated the management of specific adverse reactions (management of potential specific toxicities).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported