Clinical trial results:
Open-label Phase 2 study evaluating efficacy and safety of SAR566658 treatment in patients with CA6 positive metastatic Triple Negative Breast Cancer

Summary

EudraCT number	2016-001962-27
Trial protocol	NL BE ES FR CZ IT
Global end of trial date	07 September 2018

Results information

Result version number	v1 (current)
This version publication date	25 August 2019
First version publication date	25 August 2019

Trial information

Trial identification

Sponsor protocol code	ACT14884

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02984683
WHO universal trial number (UTN)	U1111-1182-7044

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 Avenue Pierre Brossolette, Chilly Mazarin, France, 91385
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	05 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 September 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the tumour Objective Response Rate (ORR), according to the Response Evaluation Criteria in Solid Tumours (RECIST 1.1) of SAR566658 in subjects with CA6-positive metastatic triple negative breast cancer (TNBC).
Part 1: To select the SAR566658 dose based on ORR and safety of 2 dose levels of SAR566658 in subjects with metastatic TNBC overexpressing CA6 (membrane intensity of 2+, 3+ in >=30 percent(%) of tumour cells).
Part 2: -Part 2a: To demonstrate the activity of SAR566658 based on ORR in subjects with metastatic TNBC overexpressing CA6 (membrane intensity of 2+, 3+ in >=30% of tumour cells) treated at the selected dose in an expanded cohort, in addition to the subjects treated in Part 1,
- Part 2b: To assess the efficacy of SAR566658 based on ORR in subjects with metastatic TNBC and mild CA6 expression (with at least 1% positive tumour cells at intensity >=1+ and <30% of tumour cells at intensity of 2+, 3+) treated at the selected dose in "mild CA6 expression cohort".

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 was 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 March 2017
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	Italy: 3
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czech Republic: 1
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	19
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 13 sites in 5 countries from 23 March 2017 to 07 September 2018.

Pre-assignment

Screening details:

A total of 23 subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled in the study and included in Part 1. The study was prematurely terminated due to safety reasons, hence Part 2 was not conducted and no analysis was performed.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SAR566658 90 mg/m^2

Arm description:

Subjects received SAR566658 90 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).

Arm type	Experimental
Investigational medicinal product name	SAR566658
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SAR566658 90 mg/m^2, intravenous infusion on Day 1 and 8 of each 21-day treatment cycle.

Arm title	SAR566658 120 mg/m^2

Arm description:

Subjects received SAR566658 120 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).

Arm type	Experimental
Investigational medicinal product name	SAR566658
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SAR566658 120 mg/m^2, intravenous infusion on Day 1 and 8 of each 21-day treatment cycle.

Number of subjects in period 1	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2
Started	11	12
Completed	0	0
Not completed	11	12
Disease progression	7	9
Adverse event	3	3
Withdrawal by subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	SAR566658 90 mg/m^2
Reporting group description:	
Subjects received SAR566658 90 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).	
Reporting group title	SAR566658 120 mg/m^2
Reporting group description:	
Subjects received SAR566658 120 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).	

Reporting group values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2	Total
Number of subjects	11	12	23
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	56.73	50.33	
standard deviation	± 11.23	± 15.30	-
Gender categorical Units: Subjects			
Female	11	12	23
Male	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
White	11	12	23
Black or African american	0	0	0
Asian	0	0	0
Native Hawaiian or other Pacific Island	0	0	0
Not reported	0	0	0
Unknown	0	0	0

End points

End points reporting groups

Reporting group title	SAR566658 90 mg/m^2

Reporting group description:

Subjects received SAR566658 90 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).

Reporting group title	SAR566658 120 mg/m^2

Reporting group description:

Subjects received SAR566658 120 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).

Primary: Number of Subjects With Investigational Medicinal Product (IMP)-Related Predefined Safety Criteria Findings

End point title	Number of Subjects With Investigational Medicinal Product (IMP)-Related Predefined Safety Criteria Findings[1]

End point description:

Predefined safety criteria was defined as occurrence of any following IMP-related treatment emergent adverse event (TEAE) (based on National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] v4.03): Grade >=3 TEAE from the System Organ Class (SOC) of eye disorders, Grade >=3 peripheral neuropathy (Preferred Term), Grade >=4 TEAE. Only those categories in which at least 1 subject had data were reported. Per NCI-CTCAE v4.03, Adverse Events (AE) were graded as follows: Grade 1: Mild; asymptomatic/mild symptoms; Grade 2: Moderate; minimal, local or non-invasive intervention indicated; Grade 3: Severe or medically significant; hospitalization or prolongation of hospitalization indicated; Grade 4: Life-threatening consequences; Grade 5: Death related to AE. Analysis was performed on evaluable for predefined safety criteria population which included subjects treated in the study and had completed 2 cycles, or who experienced predefined safety criteria.

End point type	Primary

End point timeframe:

Up to Cycle 2 (each cycle of 21 days)

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, hence no statistical analysis was provided.

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Subjects				
number (not applicable)				
Grade>=3 related TEAE from SOC Eye disorders	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Objective Response

End point title	Percentage of Subjects With Objective Response[2]

End point description:

Objective Response in subjects was defined as the subjects with complete response (CR) and partial response (PR) as best response according to RECIST 1.1. As per RECIST 1.1, CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 millimeter (mm). PR was defined was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Analysis was performed on all-treated population which included subjects who actually received at least 1 dose or any partial dose of SAR566658.

End point type	Primary

End point timeframe:

From Baseline, every 6 weeks until radiological disease progression or study cut-off, whichever comes first (maximum number of cycles was 3, each cycle 21 days)

Notes:

[2] - 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, hence no statistical analysis was provided.

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: percentage of subjects				
number (confidence interval 80%)	9.1 (1.0 to 31.0)	8.3 (0.9 to 28.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease Control

End point title	Percentage of Subjects With Disease Control

End point description:

Disease control in subjects was defined as the subjects with CR, PR and stable disease (SD) with a duration of at least 3 months. As per RECIST 1.1, CR was defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. SD was defined as Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (at least a 20% increase in the sum of diameters of target lesions taking as reference the smallest sum diameters while on study. Data for this endpoint was not collected and analysed due to early termination of the study.

End point type	Secondary

End point timeframe:

From Baseline, every 6 weeks until radiological disease progression or study cut-off, whichever comes first (maximum number of cycles was 3, each cycle 21 days)

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: percentage of subjects				
number (not applicable)				

Notes:

[3] - Data was not collected and analysed due to early termination of the study.

[4] - Data was not collected and analysed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

DOR was defined as the time from the first documentation of objective tumour response (CR or PR) to the first radiological documentation of tumour progression or death (due to any cause), whichever comes first. As per RECIST 1.1, CR was defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Progressive disease was defined as at least a 20% increase in the sum of diameters of target lesions. Data for this endpoint was not collected and analysed due to early termination of the study.

End point type	Secondary

End point timeframe:

From Baseline, every 6 weeks until radiological disease progression or study cut-off, whichever comes first (maximum number of cycles was 3, each cycle 21 days)

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: days				
number (not applicable)				

Notes:

[5] - Data was not collected and analysed due to early termination of the study.

[6] - Data was not collected and analysed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

PFS was defined as the time interval between the date of first study treatment administration and the date of documented tumour progression or death (due to any cause), whichever comes first. As per RECIST 1.1, Progression was defined as at least a 20% increase in the sum of diameters of target lesions. Data for this endpoint was not collected and analysed due to early termination of the study.

End point type	Secondary

End point timeframe:

From Baseline, every 6 weeks until radiological disease progression or study cut-off, whichever comes first (maximum number of cycles was 3, each cycle 21 days)

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[7]	0[8]		
Units: days				
number (not applicable)				

Notes:

[7] - Data was not collected and analysed due to early termination of the study.

[8] - Data was not collected and analysed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumour progression (TTP)

End point title	Time to Tumour progression (TTP)

End point description:

TTP was defined as the time interval between the date of first study treatment administration and the date of the first radiologically documented tumour progression. As per RECIST 1.1, progression was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. Data for this endpoint was not collected and analysed due to early termination of the study.

End point type	Secondary

End point timeframe:

From Baseline, every 6 weeks until radiological disease progression or study cut-off, whichever comes first (maximum number of cycles was 3, each cycle 21 days)

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: days				
number (not applicable)				

Notes:

[9] - Data was not collected and analysed due to early termination of the study.

[10] - Data was not collected and analysed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events and Serious Adverse Events (SAE)

End point title	Number of Subjects With Treatment Emergent Adverse Events and Serious Adverse Events (SAE)

End point description:

AE was defined as any untoward medical occurrence in a subject who received study drug and did not necessarily had a causal relationship with the treatment. TEAEs were defined as AEs that developed or worsened in grade or became serious during the on-treatment period (the time from the first treatment

administration to the last treatment administration +30 days). An SAE is any untoward medical occurrence that at any dose: results in death, Is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability / incapacity, is a congenital anomaly / birth defect, is a medically important event. Analysis was performed on all treated population.

End point type	Secondary

End point timeframe:

Up to 30 days after last drug administration

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: subjects				
number (not applicable)				
Any TEAE	11	12		
Any treatment emergent SAE	1	6		
Any TEAE leading to treatment discontinuation	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Keratopathies (corneal toxicity)

End point title	Number of Subjects with Keratopathies (corneal toxicity)

End point description:

Keratopathy is an eye disorder that involves a blister-like swelling of the cornea (the clear layer in front of the iris and pupil). All subjects received ocular primary prophylaxis in each eye in order to prevent the occurrence of keratopathies at the time of each infusion (vasoconstrictor, ophthalmic topical steroid, and cold mask on eyes) and steroid eye drops for an additional 2 days following SAR566658 administration. Analysis was performed on all treated population.

End point type	Secondary

End point timeframe:

Up to 30 days after last drug administration

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: subjects				
number (not applicable)				
Keratopathy: All Grade	3	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Positive Anti-SAR566658 Antibodies Response

End point title	Number of Subjects with Positive Anti-SAR566658 Antibodies Response

End point description:

Data for this endpoint was not collected and analysed due to early termination of the study.

End point type	Secondary

End point timeframe:

Up to 3 treatment cycles, each cycle 21 days

End point values	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	0[12]		
Units: subjects				
number (not applicable)				

Notes:

[11] - Data was not collected and analysed due to early termination of the study.

[12] - Data was not collected and analysed due to early termination of the study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data was collected from the baseline up to 3 treatment cycles, each cycle 21 days.

Adverse event reporting additional description:

Reported AEs are treatment-emergent adverse events i.e. AEs that developed/worsened during 'treatment period'(time from the first treatment administration to the last treatment administration + 30 days). Analysis was performed on safety population which included all subjects who received at least 1 dose (or any partial) of SAR566658.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	SAR566658 90 mg/m^2

Reporting group description:

Subjects received SAR566658 90 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).

Reporting group title	SAR566658 120 mg/m^2

Reporting group description:

Subjects received SAR566658 120 mg/m^2 as intravenous infusion on Day 1 and Day 8 of each 21-day treatment cycle (maximum number of cycles received was 3).

Serious adverse events	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	6 / 12 (50.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases To Meninges			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Bacteraemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			

subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SAR566658 90 mg/m^2	SAR566658 120 mg/m^2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	12 / 12 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 11 (36.36%)	3 / 12 (25.00%)	
occurrences (all)	4	3	
Device Related Thrombosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hyperthermia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Oedema Peripheral			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast Pain			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Breast Ulceration			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metrorrhagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Pleural Effusion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pulmonary Toxicity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood Bilirubin Increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Transaminases Increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Weight Decreased			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			

Intentional Overdose			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Neuropathy Peripheral			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			
subjects affected / exposed	2 / 11 (18.18%)	3 / 12 (25.00%)	
occurrences (all)	2	3	
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear Pruritus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Abnormal Sensation In Eye			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Corneal Epithelial Microcysts			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Corneal Opacity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

Diplopia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dry Eye			
subjects affected / exposed	3 / 11 (27.27%)	1 / 12 (8.33%)	
occurrences (all)	3	1	
Halo Vision			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Keratitis			
subjects affected / exposed	5 / 11 (45.45%)	1 / 12 (8.33%)	
occurrences (all)	5	1	
Keratopathy			
subjects affected / exposed	3 / 11 (27.27%)	5 / 12 (41.67%)	
occurrences (all)	3	6	
Periorbital Oedema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Photophobia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Vision Blurred			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Vitreous Floaters			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Xerophthalmia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Constipation			

subjects affected / exposed	3 / 11 (27.27%)	2 / 12 (16.67%)	
occurrences (all)	3	2	
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dry Mouth			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Odynophagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Paraesthesia Oral			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Onychomadesis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Pruritus Generalised			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 11 (18.18%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Muscle Spasms			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Neck Pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal Infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Periodontitis			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin Infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Urinary Tract Infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 11 (9.09%)	3 / 12 (25.00%)	
occurrences (all)	1	3	

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? Yes

Date	Interruption	Restart date
07 September 2018	Analysis after the first 20 subjects had been enrolled revealed a higher than expected rate of non-serious ophthalmic TEAEs identified as keratitis and keratopathy leading to dose modification and/or treatment discontinuation in both the 90 mg/m^2 and 120 mg/m^2 treatment groups which is not outweighed by a significant clinical benefit with SAR566658 and led to decision to prematurely stop the study. The corneal prophylaxis administered to all subjects does not show a positive impact on incidence of the events. The preliminary efficacy analysis indicated that the ORR was not likely to support the continuation of the study.	-

Notes:

Limitations and caveats

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

The study was prematurely terminated due to safety reasons, hence Part 2 was not conducted and no analysis was performed.

Notes: