Clinical trial results:
Ribociclib-endocrine combination therapy versus chemotherapy as 1st line treatment in patients with visceral metastatic breast cancer. A multicenter, randomized phase III trial.

Summary

EudraCT number	2018-003648-22
Trial protocol	BE AT
Global end of trial date	15 April 2021

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	SAKK_2118

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03905343
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Swiss Group for Clinical Cancer Research (SAKK)
Sponsor organisation address	Effingerstrasse 33, Bern, Switzerland, 3008
Public contact	Head Regulatory Affairs, Swiss Group for Clinical Cancer, +41 31389 91 91, sakkcc@sakk.ch
Scientific contact	Head Regulatory Affairs, Swiss Group for Clinical Cancer, +41 31389 91 91, sakkcc@sakk.ch

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	10 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 April 2021
Global end of trial reached?	Yes
Global end of trial date	15 April 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The aim of this trial is to assess if patients treated with the combination of ribociclib and endocrine therapy respond to treatment as fast as patients treated with chemotherapy only, without decreasing their quality of life (QoL).

Protection of trial subjects:

Protection of trial subjects was ensured by Safety Monitoring, i.e. assessment of adverse events, serious adverse events, adverse drug reactions, and the continous assessment of laboratory values and vital signs.

Background therapy:

None

Evidence for comparator:

Mono-chemotherapy according to local guidelines for at least 12 weeks or until progression was used as reference therapy. The choice of mono-chemotherapy was up to the investigator. It had to be registered and reimbursed by health insurances. Metronomic chemotherapy, combination chemotherapy and antiangiogenic therapy was not allowed.

Actual start date of recruitment	26 August 2019
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	Belgium: 1
Country: Number of subjects enrolled	Switzerland: 24
Worldwide total number of subjects	25
EEA total number of subjects	1

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)	10
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment phase started on 26-Aug-2019 and was prematurely stopped due to financial reasons on 25-Nov-2021 after the recruitment of 25 out of 400 planned patients. Last patient was enrolled on 12-Nov-2020. Twenty-four patients at ten centres were enrolled in Switzerland and one patient in Belgium.

Pre-assignment

Screening details:

Eligibility criteria of a patient were checked by the investigator. Once a patient fullfils all inclusion criteria and not any of the exclusion criteria, he/she was randomized.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Ribociclib and endocrine therapy. The selection of endocrine treatment was according to local guidelines and depended on registration and reimbursement by the health insurance. Endocrine therapy consisted of a registered aromatase inhibitor or fulvestrant, only if reimbursed by the health insurance.

Arm type	Experimental
Investigational medicinal product name	Ribociclib
Investigational medicinal product code	
Other name	Kisqali®
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg p.o. on day 1 to day 21, q4w

Investigational medicinal product name	Endocrine therapy (according to local quidelines)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

According to local guidelines.

Arm title	Arm B

Arm description:

Mono-chemotherapy for at least 12 weeks or until progression. Chemotherapy had to be given according to local guidelines. The choice of mono-chemotherapy was up to the investigator. It had to be registered and reimbursed by health insurances. Metronomic chemotherapy, combination chemotherapy and antiangiogenic therapy was not allowed. After at least 12 weeks and no PD, the investigator could perform a riskbenefit assessment and decide whether to continue the chemotherapy or to start a maintenance endocrine therapy with or without ribociclib.

Arm type	Active comparator

Investigational medicinal product name	Mono-chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

Chemotherapy had to be given according to local guidelines.

Number of subjects in period 1	Arm A	Arm B
Started	13	12
Completed	13	12

Period 2

Period 2 title	Treatment Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Ribociclib and endocrine therapy. The selection of endocrine treatment was according to local guidelines and depended on registration and reimbursement by the health insurance. Endocrine therapy consisted of a registered aromatase inhibitor or fulvestrant, only if reimbursed by the health insurance.

Arm type	Experimental
Investigational medicinal product name	Ribociclib
Investigational medicinal product code	
Other name	Kisqali®
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg p.o. on day 1 to day 21, q4w

Investigational medicinal product name	Endocrine therapy (according to local quidelines)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

According to local guidelines.

Arm title	Arm B

Arm description:

Mono-chemotherapy for at least 12 weeks or until progression. Chemotherapy had to be given according to local guidelines. The choice of mono-chemotherapy was up to the investigator. It had to be registered and reimbursed by health insurances. Metronomic chemotherapy, combination chemotherapy and antiangiogenic therapy was not allowed. After at least 12 weeks and no PD, the investigator could perform a riskbenefit assessment and decide whether to continue the chemotherapy or to start a maintenance endocrine therapy with or without ribociclib.

Arm type	Active comparator
Investigational medicinal product name	Mono-chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

Chemotherapy had to be given according to local guidelines.

Number of subjects in period 2	Arm A	Arm B
Started	13	12
Completed	0	0
Not completed	13	12
Physician decision	1	1
Study termination by sponsor	7	4
Progressive disease	5	6
Other - Second malignancy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Ribociclib and endocrine therapy. The selection of endocrine treatment was according to local guidelines and depended on registration and reimbursement by the health insurance. Endocrine therapy consisted of a registered aromatase inhibitor or fulvestrant, only if reimbursed by the health insurance.	
Reporting group title	Arm B
Reporting group description:	
Mono-chemotherapy for at least 12 weeks or until progression. Chemotherapy had to be given according to local guidelines. The choice of mono-chemotherapy was up to the investigator. It had to be registered and reimbursed by health insurances. Metronomic chemotherapy, combination chemotherapy and antiangiogenic therapy was not allowed. After at least 12 weeks and no PD, the investigator could perform a riskbenefit assessment and decide whether to continue the chemotherapy or to start a maintenance endocrine therapy with or without ribociclib.	

Reporting group values	Arm A	Arm B	Total
Number of subjects	13	12	25
Age categorical Units: Subjects			
Adults (18-64 years)	6	4	10
From 65-84 years	7	8	15
Gender categorical Units: Subjects			
Female	13	12	25
Male	0	0	0

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

Ribociclib and endocrine therapy. The selection of endocrine treatment was according to local guidelines and depended on registration and reimbursement by the health insurance. Endocrine therapy consisted of a registered aromatase inhibitor or fulvestrant, only if reimbursed by the health insurance.

Reporting group title	Arm B

Reporting group description:

Mono-chemotherapy for at least 12 weeks or until progression. Chemotherapy had to be given according to local guidelines. The choice of mono-chemotherapy was up to the investigator. It had to be registered and reimbursed by health insurances. Metronomic chemotherapy, combination chemotherapy and antiangiogenic therapy was not allowed. After at least 12 weeks and no PD, the investigator could perform a riskbenefit assessment and decide whether to continue the chemotherapy or to start a maintenance endocrine therapy with or without ribociclib.

Reporting group title	Arm A

Reporting group description:

Ribociclib and endocrine therapy. The selection of endocrine treatment was according to local guidelines and depended on registration and reimbursement by the health insurance. Endocrine therapy consisted of a registered aromatase inhibitor or fulvestrant, only if reimbursed by the health insurance.

Reporting group title	Arm B

Reporting group description:

Mono-chemotherapy for at least 12 weeks or until progression. Chemotherapy had to be given according to local guidelines. The choice of mono-chemotherapy was up to the investigator. It had to be registered and reimbursed by health insurances. Metronomic chemotherapy, combination chemotherapy and antiangiogenic therapy was not allowed. After at least 12 weeks and no PD, the investigator could perform a riskbenefit assessment and decide whether to continue the chemotherapy or to start a maintenance endocrine therapy with or without ribociclib.

Subject analysis set title	Arm A
Subject analysis set type	Full analysis

Subject analysis set description:

FAS = PPS
The FAS was defined as all randomized patients who received at least one dose of trial treatment excluding patients with major eligibility violations. Following the intention-to-treat principle, patients in this set were analyzed according to the treatment they were randomized to.

Subject analysis set title	Arm B
Subject analysis set type	Full analysis

Subject analysis set description:

FAS = PPS
The FAS was defined as all randomized patients who received at least one dose of trial treatment excluding patients with major eligibility violations. Following the intention-to-treat principle, patients in this set were analyzed according to the treatment they were randomized to.
One patient had a second tumor present at baseline, which was detected when the patient was already on trial treatment. The patient violated inclusion criterion 6.1.6 and was excluded from FAS (and PPS).

Primary: PE - Quality of life adjusted early disease control (composite EP - 1a/2 Disease Control - Response at week 12)

End point title	PE - Quality of life adjusted early disease control (composite EP - 1a/2 Disease Control - Response at week 12)[1]

End point description:

The primary enpoint, quality of life-adjusted early disease control at 12 weeks is a composite endpoint.
The first component is disease control (CR, PR or SD according to RECIST v1.1) at 12 weeks (+1 week for delayed assessments).
If a patient had no assessment at 12 weeks but CR, PR or SD thereafter it was counted as SD at 12 weeks.
The second component was defined as follows: FACTB TOI score does not worsen by 5 points or more during the first 12 weeks after randomization (+1 week for delayed assessments).

End point type	Primary

End point timeframe:

Responses at week 12

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: Due to the low sample size, statistical analysis was not performed and data were analyzed descriptively.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (not applicable)				
Partial response (PR)	30.8	27.3		
Stable disease (SD)	69.2	54.5		
Progressive disease (PD)	0	9.1		
Not evaluable (NA)	0	9.1		

Statistical analyses

No statistical analyses for this end point

Primary: PE - Quality of life adjusted early disease control (composite EP - 1b/2 Disease Control - Disease control at week 12)

End point title	PE - Quality of life adjusted early disease control (composite EP - 1b/2 Disease Control - Disease control at week 12)[2]

End point description:

The primary enpoint, quality of life-adjusted early disease control at 12 weeks is a composite endpoint. The first component is disease control (CR, PR or SD according to RECIST v1.1) at 12 weeks (+1 week for delayed assessments).
If a patient had no assessment at 12 weeks but CR, PR or SD thereafter it was counted as SD at 12 weeks.
The second component was defined as follows: FACTB TOI score does not worsen by 5 points or more during the first 12 weeks after randomization (+1 week for delayed assessments).

End point type	Primary

End point timeframe:

Disease control at week 12.

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: Due to the low sample size, statistical analysis was not performed and data were analyzed descriptively.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (not applicable)				
Yes	100	81.8		
No	0	18.2		

Statistical analyses

No statistical analyses for this end point

Primary: PE - Quality of life adjusted early disease control (composite EP - 2/2 FACT-B TOI worsening during first 12 weeks)

End point title	PE - Quality of life adjusted early disease control (composite EP - 2/2 FACT-B TOI worsening during first 12 weeks)[3]

End point description:

The primary enpoint, quality of life-adjusted early disease control at 12 weeks is a composite endpoint.
The first component is disease control (CR, PR or SD according to RECIST v1.1) at 12 weeks (+1 week for delayed assessments).
If a patient had no assessment at 12 weeks but CR, PR or SD thereafter it was counted as SD at 12 weeks.
The second component was defined as follows: FACTB TOI score does not worsen by 5 points or more during the first 12 weeks after randomization (+1 week for delayed assessments).

End point type	Primary

End point timeframe:

TOI worsening of at least 5 points within first 12 weeks

Notes:

[3] - 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: Due to the low sample size, statistical analysis was not performed and data were analyzed descriptively.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (not applicable)				
No	53.8	54.5		
Yes	38.5	45.5		
NA	7.7	0		

Statistical analyses

No statistical analyses for this end point

Primary: PE - Quality of life adjusted early disease control (composite EP - Composite)

End point title	PE - Quality of life adjusted early disease control (composite EP - Composite)[4]

End point description:

The primary enpoint, quality of life-adjusted early disease control at 12 weeks is a composite endpoint.
The first component is disease control (CR, PR or SD according to RECIST v1.1) at 12 weeks (+1 week for delayed assessments).
If a patient had no assessment at 12 weeks but CR, PR or SD thereafter it was counted as SD at 12

weeks.
The second component was defined as follows: FACTB TOI score does not worsen by 5 points or more during the first 12 weeks after randomization (+1 week for delayed assessments).

End point type	Primary

End point timeframe:

Composite of quality of life-adjusted disease control at week 12

Notes:

[4] - 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: Due to the low sample size, statistical analysis was not performed and data were analyzed descriptively.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (not applicable)				
Yes	53.8	45.5		
No	46.2	54.5		

Statistical analyses

No statistical analyses for this end point

Primary: PE - Quality of life adjusted early disease control (composite EP - Composite rate)

End point title	PE - Quality of life adjusted early disease control (composite EP - Composite rate)[5]

End point description:

The primary enpoint, quality of life-adjusted early disease control at 12 weeks is a composite endpoint. The first component is disease control (CR, PR or SD according to RECIST v1.1) at 12 weeks (+1 week for delayed assessments).
If a patient had no assessment at 12 weeks but CR, PR or SD thereafter it was counted as SD at 12 weeks.
The second component was defined as follows: FACTB TOI score does not worsen by 5 points or more during the first 12 weeks after randomization (+1 week for delayed assessments).

End point type	Primary

End point timeframe:

Composit quality of life-adjusted disease control rate at week 12

Notes:

[5] - 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: Due to the low sample size, statistical analysis was not performed and data were analyzed descriptively.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (confidence interval 95%)	53.8 (25.1 to 80.8)	45.5 (16.7 to 76.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: SE - Disease control at week 12

End point title	SE - Disease control at week 12

End point description:

Disease control at week 12 (see also primary endpoint)

End point type	Secondary

End point timeframe:

12 weeks

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (confidence interval 95%)	100.0 (75.3 to 100.0)	81.8 (48.2 to 97.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: SE - Objective response rate (ORR) 1/2 Best overall response

End point title	SE - Objective response rate (ORR) 1/2 Best overall response

End point description:

Best overall response according to RECIST v1.1, i.e. CR/PR rates

End point type	Secondary

End point timeframe:

From Baseline until EoS

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (not applicable)				
Complete remission (CR)	0	0		
Partial response (PR)	61.5	36.4		
Stable disease (SD)	38.5	63.6		

Statistical analyses

No statistical analyses for this end point

Secondary: SE - Objective response rate (ORR) 2/2 Objective response rate

End point title	SE - Objective response rate (ORR) 2/2 Objective response rate
End point description: Objective response rate	
End point type	Secondary
End point timeframe: From baseline until EoS.	

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Patients (%)				
number (confidence interval 95%)	61.5 (31.6 to 86.1)	36.4 (10.9 to 69.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: SE - Objective response rate (ORR) - Time to objective response

End point title	SE - Objective response rate (ORR) - Time to objective response
End point description: Time to event analysis (Kaplan-Meier) for patient with ORR partial response; 8 patients in arm A and 4 in arm B reached PR.	
End point type	Secondary
End point timeframe: Time to event from enrollment.	

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13[6]	11[7]		
Units: Months				
median (full range (min-max))	4.1 (1.1 to 8.1)	1.9 (0.9 to 8.2)		

Notes:

[6] - Analysis only for patients with ORR = PR.

[7] - Analysis only for patients with ORR = PR.

Statistical analyses

No statistical analyses for this end point

Secondary: SE - Progression-free survival (PFS)

End point title	SE - Progression-free survival (PFS)

End point description:

Time to event analysis (Kaplan-Meier) for progression-free survival (PFS); 6 patients in arm A and 6 in arm B had experienced disease progression.
NOTE: UPPER LIMITS FOR 95% CI FOR MEDIAN PFS WERE NOT REACHED. HOWEVER, DUMMY VALUES FOR UPPER 95% CI LIMITS ENTERED DUE TO DATABASE RESTRICTIONS.

End point type	Secondary

End point timeframe:

Time to event from enrollment.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Months				
median (confidence interval 95%)	11.0 (5.5 to 100000)	10.6 (2.6 to 100000)		

Statistical analyses

No statistical analyses for this end point

Secondary: SE - Time to treatment failure (TTF)

End point title	SE - Time to treatment failure (TTF)

End point description:

Time to event analysis (Kaplan-Meier) for time to treatment failure (TTF); all patients stopped trial treatment before the planned 3 years of treatment. One patient in arm A and one in arm B were treated beyond progression (see Section 6.5). For these patients TTF was longer than PFS.

End point type	Secondary

End point timeframe:

Time to event from enrollment.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Months				
median (confidence interval 95%)	10.2 (6.4 to 11.4)	5.7 (2.6 to 12.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: SE - Overall survival (OS)

End point title	SE - Overall survival (OS)

End point description:

Time to event analysis (Kaplan-Meier) for overall survival (OS); two patients in arm A and one patient in arm B had died.
NOTE: MEDIAN OS TIMES WERE NOT REACHED. DUMMY DATA ENTERED DUE TO DATABASE RESTRICTIONS.

End point type	Secondary

End point timeframe:

Time to event from enrollment.

End point values	Arm A	Arm B		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Months				
median (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From enrollment until EoS.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Arm A (SAF)
Reporting group description: -	
Reporting group title	Arm B (SAF)
Reporting group description: -	

Serious adverse events	Arm A (SAF)	Arm B (SAF)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	2 / 12 (16.67%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal carcinoma			
subjects affected / exposed	0 / 13 (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	
Vascular disorders			
Embolism			
subjects affected / exposed	3 / 13 (23.08%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 13 (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			
Gastritis			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine hemorrhage			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lung infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A (SAF)	Arm B (SAF)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 13 (53.85%)	8 / 12 (66.67%)	

Investigations			
Neutrophil count decreased			
subjects affected / exposed	6 / 13 (46.15%)	1 / 12 (8.33%)	
occurrences (all)	13	4	
Platelet count decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
White blood cell count decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Embolism arterial			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Embolism			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Urticaria			

subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	

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.

The study was terminated prematurely by the sponsor. All patients stopped trial treatment before the planned three years of treatment. The sample size was low (planned 400 patients; actual: 25 patients). Thus data have to be interpreted with caution.

Notes: