Clinical trial results:
A phase 2, open-label, single-arm, multicenter study to evaluate the efficacy and safety of SOT101 in combination with cetuximab in patients with RAS wild-type colorectal cancer (AURELIO-05)

Summary

EudraCT number	2022-001527-32
Trial protocol	ES BE IT FR
Global end of trial date	03 June 2024

Results information

Result version number	v1 (current)
This version publication date	30 May 2025
First version publication date	30 May 2025

Trial information

Trial identification

Sponsor protocol code	SC105 (AURELIO-05)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05619172
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 140011

Notes:

Sponsors

Sponsor organisation name	SOTIO Biotech AG
Sponsor organisation address	Lichtstrasse 35 - WSJ-210, Basel, Switzerland, 4056
Public contact	Clinical trials, SOTIO Biotech AG, +420 224 175 111, clinicaltrial@sotio.com
Scientific contact	Clinical trials, SOTIO Biotech AG, +420 224 175 111, clinicaltrial@sotio.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	03 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2024
Global end of trial reached?	Yes
Global end of trial date	03 June 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To estimate the antitumor efficacy of nanrilkefusp alfa in combination with cetuximab

Protection of trial subjects:

Not applicable

Background therapy:

Cetuximab was administered on day 1 (from cycle 2 onwards, ±1 day), day 8 (±1 day), and day 15 (±1 day) of each 21-day cycle. The initial dose of cetuximab was 400 mg/m2 body surface area administered as intravenous infusion over 120 minutes. All subsequent weekly doses were 250 mg/m2 each administered as intravenous infusion over 60 minutes. Patients may have been premedicated with an antihistamine and a corticosteroid at least 1 hour before cetuximab administration. On day 1 and day 8, cetuximab infusion started within 30 minutes after nanrilkefusp alfa administration.

Evidence for comparator:

Not applicable

Actual start date of recruitment	22 December 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	France: 3
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	11
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Not applicable

Pre-assignment

Screening details:

Eight investigational sites participated in study SC105 and screened at least 1 patient (2 sites in France, 4 sites in Spain, and 2 sites in Belgium).

Period 1

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

Arms

Arm title	Nanrilkefusp alfa combined with cetuximab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Nanrilkefusp alfa
Investigational medicinal product code	SOT101
Other name	SO-C101, RLI-15
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Subcutaneous use

Dosage and administration details:

Nanrilkefusp alfa was administered subcutaneously on day 1 (from cycle 2 onwards, ±1 day), day 2 (±1 day), day 8 (±1 day), and day 9 (±1 day) of each 21-day cycle. The dose of nanrilkefusp alfa for the main cohort of the study was determined in the initial 3+3 safety cohorts.

Number of subjects in period 1	Nanrilkefusp alfa combined with cetuximab
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Overall (overall period)

Reporting group description: -

Reporting group values	Overall (overall period)	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	11	
From 65-84 years	5	5	
85 years and over	0	0	
Age continuous Units: years			
median	60.0		
full range (min-max)	40 to 74	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	10	10	

Subject analysis sets

Subject analysis set title	All-subjects-as-treated population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The all-subjects-as-treated (ASaT) population consisted of all patients exposed to nanrilkefusp alfa or cetuximab. All safety analyses and selected efficacy analyses were performed on the ASaT population.

Reporting group values	All-subjects-as-treated population		
Number of subjects	16		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	11		
From 65-84 years	5		
85 years and over	0		
Age continuous			
Units: years			
median	60.0		
full range (min-max)	40 to 74		
Gender categorical			
Units: Subjects			
Female	6		
Male	10		

End points

End points reporting groups

Reporting group title	Nanrilkefusp alfa combined with cetuximab
Reporting group description: -	
Subject analysis set title	All-subjects-as-treated population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The all-subjects-as-treated (ASaT) population consisted of all patients exposed to nanrilkefusp alfa or cetuximab. All safety analyses and selected efficacy analyses were performed on the ASaT population.

Primary: Objective response rate according to RECIST 1.1

End point title	Objective response rate according to RECIST 1.1[1]

End point description:

Objective response rate according to RECIST 1.1 was defined as the proportion of patients with complete response according to RECIST 1.1 or partial response according to RECIST 1.1. Patients with missing data were considered non-responders.

End point type	Primary

End point timeframe:

Day 1 up to approximately 3 years

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: No statistical analysis was planned for this end point.

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percent				
number (confidence interval 95%)	0 (0 to 20.591)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate according to iRECIST

End point title	Objective response rate according to iRECIST

End point description:

Objective response rate according to iRECIST was defined as the proportion of patients with complete response according to iRECIST or partial response according to iRECIST. Patients with missing data were considered non-responders.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percent				
number (confidence interval 95%)	0 (0 to 20.591)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to RECIST 1.1: complete response

End point title	Best overall response according to RECIST 1.1: complete response

End point description:

The best overall response according to RECIST 1.1 was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to RECIST 1.1 had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to RECIST 1.1: partial response

End point title	Best overall response according to RECIST 1.1: partial response

End point description:

The best overall response according to RECIST 1.1 was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to RECIST 1.1 had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to RECIST 1.1: stable disease

End point title	Best overall response according to RECIST 1.1: stable disease

End point description:

The best overall response according to RECIST 1.1 was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to RECIST 1.1 had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to RECIST 1.1: progressive disease

End point title	Best overall response according to RECIST 1.1: progressive disease

End point description:

The best overall response according to RECIST 1.1 was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to RECIST 1.1 had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to iRECIST: complete response

End point title	Best overall response according to iRECIST: complete response

End point description:

The best overall response according to iRECIST was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to iRECIST had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to iRECIST: partial response

End point title	Best overall response according to iRECIST: partial response

End point description:

The best overall response according to iRECIST was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to iRECIST had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to iRECIST: stable disease

End point title	Best overall response according to iRECIST: stable disease

End point description:

The best overall response according to iRECIST was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to iRECIST had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to iRECIST: unconfirmed progressive disease

End point title	Best overall response according to iRECIST: unconfirmed progressive disease

End point description:

The best overall response according to iRECIST was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to iRECIST had to last at least 6 weeks from the start of study treatment. If

not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response according to iRECIST: confirmed progressive disease

End point title	Best overall response according to iRECIST: confirmed progressive disease

End point description:

The best overall response according to iRECIST was defined as the best response from the start of study treatment until the first documented disease progression, death, or start of new anti-cancer therapy. Stable disease according to iRECIST had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response according to RECIST 1.1

End point title	Duration of response according to RECIST 1.1

End point description:

Duration of response according to RECIST 1.1 was defined as time to disease progression for patients with partial response or complete response according to RECIST 1.1.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response according to iRECIST

End point title	Duration of response according to iRECIST

End point description:

Duration of response according to iRECIST was defined as time to disease progression for patients with partial response or complete response according to iRECIST.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical benefit rate according to RECIST 1.1

End point title	Clinical benefit rate according to RECIST 1.1

End point description:

Clinical benefit rate according to RECIST 1.1 was defined as the number of partial responses, complete responses, and stable disease according to RECIST 1.1. Stable disease had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease. Patients with missing data were considered non-responders.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percent				
number (confidence interval 95%)	37.5 (15.198 to 64.565)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical benefit rate according to iRECIST

End point title	Clinical benefit rate according to iRECIST

End point description:

Clinical benefit rate according to iRECIST was defined as the number of partial responses, complete responses, and stable disease according to iRECIST. Stable disease had to last at least 6 weeks from the start of study treatment. If not, at least 1 follow-up scan was required to declare stable disease. Patients with missing data were considered non-responders.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percent				
number (confidence interval 95%)	37.5 (15.198 to 64.565)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival according to RECIST 1.1

End point title	Progression-free survival according to RECIST 1.1

End point description:

Progression-free survival according to RECIST 1.1 was defined as the time from the first day of study treatment to the first date of radiological disease progression according to RECIST 1.1 or death.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	2.7 (1.05 to 3.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival according to iRECIST

End point title	Progression-free survival according to iRECIST

End point description:

Progression-free survival according to iRECIST was defined as the time from the first day of study treatment to the first date of radiological disease progression according to iRECIST or death.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	2.7 (1.05 to 3.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response according to RECIST 1.1

End point title	Time to response according to RECIST 1.1

End point description:

Time to response according to RECIST 1.1 was defined as the time from the first day of study treatment to the first date of partial response or complete response according to RECIST 1.1. Patients with missing data were censored at the last assessment date, date of death, or date of eligibility (for incomplete or missing baseline tumor assessments), whichever occurred last.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response according to iRECIST

End point title	Time to response according to iRECIST

End point description:

Time to response according to iRECIST was defined as the time from the first day of study treatment to the first date of partial response or complete response according to iRECIST. Patients with missing data were censored at the last assessment date, date of death, or date of eligibility (for incomplete or missing baseline tumor assessments), whichever occurred last.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression according to RECIST 1.1

End point title	Time to progression according to RECIST 1.1

End point description:

Time to progression according to RECIST 1.1 was defined as the time from the first day of study treatment to the first date of radiological disease progression according to RECIST 1.1.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	2.8 (1.35 to 3.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression according to iRECIST

End point title	Time to progression according to iRECIST

End point description:

Time to progression according to iRECIST was defined as the time from the first day of study treatment to the first date of radiological disease progression according to iRECIST.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Months				
median (confidence interval 95%)	2.8 (1.35 to 3.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with treatment-emergent adverse events

End point title	Number of patients with treatment-emergent adverse events

End point description:

A treatment-emergent adverse event was defined as an adverse event that started or worsened at or after the start of study treatment.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with clinical laboratory test abnormalities

End point title	Number of patients with clinical laboratory test abnormalities

End point description:

The following laboratory parameters were assessed:
Coagulation: prothrombin time, activated partial thromboplastin time, international normalized ratio, D-dimer, and fibrinogen
Hematology: hemoglobin, hematocrit, red blood cell count, reticulocytes, white blood cell count (with full differentiation), absolute lymphocyte count, and platelet count
Clinical chemistry: Na, K, Cl, phosphate, Mg, Ca, albumin, total protein, ALT, AST, bilirubin (direct, total), alkaline phosphatase, lactate dehydrogenase, creatinine clearance calculated by the Cockcroft-Gault formula, creatinine, glucose (preferably fasting), urea or blood urea nitrogen, cholesterol, triglyceride, C-reactive protein, uric acid, amylase, and lipase
Urinalysis: pH, glucose, protein, bilirubin, urobilinogen. Microscopic examination (mandated only if clinically indicated): red blood cell count, white blood cell count, epithelial cells, bacteria

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with vital signs abnormalities

End point title	Number of patients with vital signs abnormalities

End point description:

The following vital signs parameters were assessed: Blood pressure (systolic and diastolic, after ≥5 minutes of rest), body temperature, and heart rate

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with electrocardiography abnormalities

End point title	Number of patients with electrocardiography abnormalities

End point description:

Standard 12-lead electrocardiography was evaluated locally.

End point type	Secondary

End point timeframe:

Day 1 up to approximately 3 years

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with dose-limiting toxicities

End point title	Number of patients with dose-limiting toxicities

End point description:

The following adverse events as per NCI CTCAE version 5.0 were considered dose-limiting toxicities:
- All grade 5 events not clearly related to disease progression or any other causes
- Any grade 3 or higher non-hematologic toxicity regardless of duration; exceptions:
-- Grade 3 nausea, vomiting, or diarrhea that could be controlled within 72 hours
-- Grade 3 fatigue lasting less than 5 days
-- Grade 3 or higher correctable electrolyte abnormalities lasting less than 72 hours and not associated with clinical complications
-- Grade 3 or higher serum amylase or lipase not associated with clinical manifestations of pancreatitis
-- Grade 3 AST or ALT increase or grade 3 blood bilirubin increase lasting 5 days or less
- Hy's law cases
- Hematologic DLTs:
-- Grade 4 decreased neutrophil count or decreased platelet count lasting more than 7 days
-- Febrile neutropenia
-- Grade 3 or higher decreased platelet count with bleeding

End point type	Secondary

End point timeframe:

Through Cycle 1 (21 days)

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Patients	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve of nanrilkefusp alfa

End point title	Area under the curve of nanrilkefusp alfa

End point description: At 9 µg/kg nanrilkefusp alfa, over the last measurable timepoint	
End point type	Secondary
End point timeframe: Day 1 of Cycle 1	

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: h*ng/mL				
median (full range (min-max))	37.1 (21.8 to 88.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration of nanrilkefusp alfa

End point title	Maximum concentration of nanrilkefusp alfa
End point description: At 9 µg/kg nanrilkefusp alfa	
End point type	Secondary
End point timeframe: Day 1 of Cycle 1	

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: ng/mL				
median (full range (min-max))	3.56 (1.45 to 6.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to maximum concentration of nanrilkefusp alfa

End point title	Time to maximum concentration of nanrilkefusp alfa

End point description: At 9 µg/kg nanrilkefusp alfa	
End point type	Secondary
End point timeframe: Day 1 of Cycle 1	

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Hours				
median (full range (min-max))	6.21 (2.03 to 22.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose concentration of nanrilkefusp alfa

End point title	Pre-dose concentration of nanrilkefusp alfa
End point description: At 9 µg/kg nanrilkefusp alfa	
End point type	Secondary
End point timeframe: Day 1 of Cycle 1	

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: ng/mL				
median (full range (min-max))	0.404 (0.178 to 1.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment-induced anti-drug antibodies against nanrilkefusp alfa

End point title	Incidence of treatment-induced anti-drug antibodies against

	nanrilkefusp alfa

End point description:

At 9 µg/kg and 12 µg/kg nanrilkefusp alfa

End point type	Secondary

End point timeframe:

Day 1 until 30 (±2) days after the last dose of nanrilkefusp alfa

End point values	Nanrilkefusp alfa combined with cetuximab			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Patients	5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events: from the start to 90 days after the end of study treatment; related serious adverse events: collected beyond 90 days after the end of study treatment; deaths: consent signature to study end

Adverse event reporting additional description:

Only treatment-emergent adverse events were analyzed (see the definition above); the tables include information on treatment-emergent adverse events, serious treatment-emergent adverse events, and all deaths; causality was assessed by investigators

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Nanrilkefusp alfa combined with cetuximab

Reporting group description: -

Serious adverse events	Nanrilkefusp alfa combined with cetuximab		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 16 (50.00%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	6		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood bilirubin increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Disease progression				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
General physical health deterioration				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Device related infection				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Nanrilkefusp alfa combined with cetuximab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	4		
Raynaud's phenomenon			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 16 (68.75%)		
occurrences (all)	13		
Pyrexia			
subjects affected / exposed	10 / 16 (62.50%)		
occurrences (all)	28		
Injection site reaction			
subjects affected / exposed	7 / 16 (43.75%)		
occurrences (all)	7		
Chills			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	7		
Immune system disorders			

Cytokine release syndrome subjects affected / exposed occurrences (all) Hypersensitivity subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Pleural effusion subjects affected / exposed occurrences (all)	 3 / 16 (18.75%) 3 2 / 16 (12.50%) 2 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Irritability subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all)	 4 / 16 (25.00%) 4 3 / 16 (18.75%) 4		

Blood bilirubin increased subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Amylase increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
C-reactive protein increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3		
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Dysgeusia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Headache subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		

Paraesthesia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	6 / 16 (37.50%) 9		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	6 / 16 (37.50%) 7		
Nausea subjects affected / exposed occurrences (all)	6 / 16 (37.50%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 5		
Abdominal pain subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 4		
Stomatitis subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 4		
Constipation subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Dry mouth subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Flatulence			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oesophagitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oral dysaesthesia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	8 / 16 (50.00%)		
occurrences (all)	11		
Rash			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Dry skin			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Erythema			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin toxicity			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Muscular weakness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	4		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
COVID-19			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Candida infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Paronychia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Wound infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	7		
Decreased appetite			

subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Hypoalbuminaemia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Hypophosphataemia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2023	- Addition of a urine pregnancy test to the End of treatment visit and in the Follow-up - Timing of body weight assessment used for calculation of dose clarified to be made within 3 days prior to day 1 - Addition of ECG assessment to day 1 of each cycle and End of treatment visit - Allowed visit window for safety laboratory samples adjusted - Collection of samples for ADA determination in the treatment phase limited to cycles 2, 3 and 4 - Initial tumor scans can be taken with a visit window of 21 days before ICF signature - PK sampling schedule adjusted - Benefit/risk assessment updated - PK and immunogenicity of cetuximab are to be determined as an exploratory endpoint - Inclusion criterion 5 was modified, and criterion no. 6 was added with specification of tests to be used for confirmation of RAS wild type - Inclusion criterion 6 on EGFR mutation status availability was removed, information on status determination added into another section - Exclusion criterion 4 added to specify allowed lines of previous therapy to four - Addition of management recommendations for cytokine release syndrome, shortening of the QT interval, increased ALT and/or AST, and injection site reaction - Guidance added on additional diagnostic measurements for patients with pre-existing pulmonary diseases and/or presence or suspicion of ILD and for patients with ophthalmological pre-conditions - Clarification added that safety assessments are to be done by local laboratories - Hy’s law added and referred to in appendix 3 - Cockcroft-Gault formula added and referred to in appendix 4 - Sample size of patients specified to include patients from the safety cohorts and the main cohort - Change of “SOT101” to “nanrilkefusp alfa in Protocol body

Notes:

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.

None reported

Notes: