



Clinical trial results:

A dose escalation and phase IIa study of TG6002 plus flucytosine in patients with unresectable colorectal cancer with liver metastases

Summary

EudraCT number	2018-004103-39
Trial protocol	GB FR
Global end of trial date	23 February 2023

Results information

Result version number	v1 (current)
This version publication date	23 February 2024
First version publication date	23 February 2024

Trial information

Trial identification

Sponsor protocol code	TG6002.03
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04194034
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	TRANSGENE S.A.
Sponsor organisation address	400 boulevard Gonther d'Andernach - Parc d'innovation - CS80166, Illkirch-Graffenstaden, France, 67405
Public contact	Medical Affairs, TRANSGENE S.A., 33 388279155, clinical.trials@transgene.fr
Scientific contact	Medical Affairs, TRANSGENE S.A., 33 388279155, clinical.trials@transgene.fr

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	19 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2022
Global end of trial reached?	Yes
Global end of trial date	23 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the phase I part is to determine the maximum tolerated dose (MTD) of TG6002 or maximal feasible dose (MFD) and the recommended dose for the Phase II part (RP2D) for TG6002 administered as an intrahepatic artery (IHA) infusions in combination with flucytosine (5-FC) in patients with unresectable advanced metastatic colorectal cancer (CRC) with liver metastases.

Secondary objectives include the assessment of the safety and tolerability of TG6002 administration by selective IHA infusion combined with oral 5-FC, the assessment of the study treatment efficacy and the assessment of TG6002 viral shedding.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy:

Not applicable.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	17 January 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Regulatory reason
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	France: 8
Worldwide total number of subjects	15
EEA total number of subjects	8

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	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First participant signed informed consent on 17 January 2020. Last participant last visit occurred on 1 August 2022, before long term follow-up.

Pre-assignment

Screening details:

Of 20 screened participants, 15 were included in the trial and 5 patients were excluded (4 because they were ineligible and 1 due to logistical constraints during the covid-19 pandemic).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	1 x 10E6 pfu

Arm description:

Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E6 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.

Arm type	Experimental
Investigational medicinal product name	5-FC
Investigational medicinal product code	
Other name	Ancotil
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were given oral 5-FC at 200 mg/kg/day from Day 5 to 14 (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose given on Days 47 to 56.

Investigational medicinal product name	TG6002
Investigational medicinal product code	TG6002
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intraarterial use

Dosage and administration details:

Patients were administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E6 pfu (single dose on Day 1) in combination with oral 5-FC (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose with an IHA infusion of TG6002 on Day 43 (+ 7 days) and oral 5-FC.

Arm title	1 x 10E7 pfu
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Arm description:

Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E7 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.

Arm type	Experimental
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Investigational medicinal product name	5-FC
Investigational medicinal product code	
Other name	Ancotil
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were given oral 5-FC at 200 mg/kg/day from Day 5 to 14 (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose given on Days 47 to 56.

Investigational medicinal product name	TG6002
Investigational medicinal product code	TG6002
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intraarterial use

Dosage and administration details:

Patients were administered with TG6002 intrahepatic artery (IHA) infusion at 1×10^7 pfu (single dose on Day 1) in combination with oral 5-FC (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose with an IHA infusion of TG6002 on Day 43 (+ 7 days) and oral 5-FC.

Arm title	1 x 10E8 pfu
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Arm description:

Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1×10^8 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.

Arm type	Experimental
Investigational medicinal product name	5-FC
Investigational medicinal product code	
Other name	Ancotil
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were given oral 5-FC at 200 mg/kg/day from Day 5 to 14 (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose given on Days 47 to 56.

Investigational medicinal product name	TG6002
Investigational medicinal product code	TG6002
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intraarterial use

Dosage and administration details:

Patients were administered with TG6002 intrahepatic artery (IHA) infusion at 1×10^8 pfu (single dose on Day 1) in combination with oral 5-FC (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose with an IHA infusion of TG6002 on Day 43 (+ 7 days) and oral 5-FC.

Arm title	1 x 10E9 pfu
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Arm description:

Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1×10^9 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.

Arm type	Experimental
Investigational medicinal product name	5-FC
Investigational medicinal product code	
Other name	Ancotil
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were given oral 5-FC at 200 mg/kg/day from Day 5 to 14 (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose given on Days 47 to 56.

Investigational medicinal product name	TG6002
Investigational medicinal product code	TG6002
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intraarterial use

Dosage and administration details:

Patients were administered with TG6002 intrahepatic artery (IHA) infusion at 1×10^9 pfu (single dose on Day 1) in combination with oral 5-FC (Cycle 1). If there was no disease progression or occurrence of toxicity that would jeopardize the patient study participation, the patient was proposed a second cycle of TG6002 plus 5-FC at the same dose with an IHA infusion of TG6002 on Day 43 (+ 7 days) and oral 5-FC.

Number of subjects in period 1	1 x 10E6 pfu	1 x 10E7 pfu	1 x 10E8 pfu
Started	3	3	3
Completed	3	3	3
Not completed	0	0	0
Adverse event, non-fatal	-	-	-
For best supportive care	-	-	-

Number of subjects in period 1	1 x 10E9 pfu
Started	6
Completed	4
Not completed	2
Adverse event, non-fatal	1
For best supportive care	1

Baseline characteristics

Reporting groups

Reporting group title	1 x 10E6 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E6 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	
Reporting group title	1 x 10E7 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E7 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	
Reporting group title	1 x 10E8 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E8 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	
Reporting group title	1 x 10E9 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E9 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	

Reporting group values	1 x 10E6 pfu	1 x 10E7 pfu	1 x 10E8 pfu
Number of subjects	3	3	3
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	1	2
From 65-84 years	1	2	1
85 years and over	0	0	0
Age continuous			
Units: years			
median	61	68	53
full range (min-max)	59 to 70	59 to 77	37 to 69
Gender categorical			
Units: Subjects			
Female	0	1	0
Male	3	2	3
ECOG performance status			
Units: Subjects			
Score 0	3	2	3
Score 1	0	1	0
Score 2	0	0	0
Score 3	0	0	0
Score 4	0	0	0
Tumor stage at initial diagnosis			

Units: Subjects			
Stage IA	0	0	0
Stage IB	0	0	0
Stage IIA	0	0	0
Stage IIB	0	0	0
Stage IIIA	0	0	0
Stage IIIB	1	0	0
Stage IIIC	0	1	0
Stage IV	2	2	3
Primary location of disease			
Units: Subjects			
Colon	2	2	3
Rectum	1	1	0

Reporting group values	1 x 10E9 pfu	Total	
Number of subjects	6	15	
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)	5	10	
From 65-84 years	1	5	
85 years and over	0	0	
Age continuous			
Units: years			
median	59.5		
full range (min-max)	50 to 78	-	
Gender categorical			
Units: Subjects			
Female	3	4	
Male	3	11	
ECOG performance status			
Units: Subjects			
Score 0	1	9	
Score 1	5	6	
Score 2	0	0	
Score 3	0	0	
Score 4	0	0	
Tumor stage at initial diagnosis			
Units: Subjects			
Stage IA	0	0	
Stage IB	0	0	
Stage IIA	0	0	
Stage IIB	0	0	
Stage IIIA	0	0	
Stage IIIB	0	1	

Stage IIIC	1	2	
Stage IV	5	12	
Primary location of disease Units: Subjects			
Colon	4	11	
Rectum	2	4	

End points

End points reporting groups

Reporting group title	1 x 10E6 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E6 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	
Reporting group title	1 x 10E7 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E7 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	
Reporting group title	1 x 10E8 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E8 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	
Reporting group title	1 x 10E9 pfu
Reporting group description: Cohort of patients administered with TG6002 intrahepatic artery (IHA) infusion at 1 x 10E9 pfu in combination with oral 5-FC at 200 mg/kg/day for 10 days.	

Primary: Safety and tolerability of TG6002 and 5-FC

End point title	Safety and tolerability of TG6002 and 5-FC ^[1]
End point description: Patients were assessed for dose limiting toxicities (DLT) as well as for safety and tolerability of the treatment.	
End point type	Primary
End point timeframe: Patients were assessed for dose limiting toxicity (DLTs) occurring within 28 days of administration of the first TG6002 infusion.	
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: Data for this end point were analyzed descriptively.	

End point values	1 x 10E6 pfu	1 x 10E7 pfu	1 x 10E8 pfu	1 x 10E9 pfu
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: Events				
Dose Limiting Toxicities (DLTs)	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were recorded from the first IMP admin. up to 28 days after the last IMP admin.

SAE related to study treatment were recorded with no time limitation.

SAEs related to a protocol procedure were recorded from the time of ICF signature.

Adverse event reporting additional description:

Adverse event information was collected by regular investigator assessment and regular laboratory testing.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	1 x 10E6 pfu
Reporting group description: -	
Reporting group title	1 x 10E7 pfu
Reporting group description: -	
Reporting group title	1 x 10E8 pfu
Reporting group description: -	
Reporting group title	1 x 10E9 pfu
Reporting group description: -	
Reporting group title	Safety population
Reporting group description:	
Participants who received at least one dose of either IMP.	

Serious adverse events	1 x 10E6 pfu	1 x 10E7 pfu	1 x 10E8 pfu
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	3	3	3
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Vascular procedure complication	Additional description: Pre-drug event related to other study procedure		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	1 x 10E9 pfu	Safety population	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	3 / 15 (20.00%)	
number of deaths (all causes)	4	13	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Vascular procedure complication	Additional description: Pre-drug event related to other study procedure		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	1 x 10E6 pfu	1 x 10E7 pfu	1 x 10E8 pfu
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	2 / 3 (66.67%)
Vascular disorders			
Hypertension	Additional description: Hypertension		
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Chills	Additional description: Chills		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort	Additional description: Chest discomfort		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Asthenia	Additional description: Asthenia		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0

Psychiatric disorders			
Depression	Additional description: Depression		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Anxiety	Additional description: Anxiety		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amylase increased	Additional description: Amylase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood bicarbonate increased	Additional description: Blood bicarbonate increased		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Mean cell volume abnormal	Additional description: Mean cell volume abnormal		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased	Additional description: Blood creatinine increased		

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased	Additional description: Blood creatine phosphokinase increased		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache	Additional description: Headache		
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	6	0	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	6	1	0
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Frequent bowel movements	Additional description: Frequent bowel movements		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Vomiting	Additional description: Vomiting		

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Hepatobiliary disorders			
Hepatic pain	Additional description: Hepatic pain		
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Night sweats	Additional description: Night sweats		
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Back pain	Additional description: Back pain		
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Myalgia	Additional description: Myalgia		
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Infections and infestations			
Cystitis	Additional description: Cystitis		
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Metabolism and nutrition disorders			
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Hyperkalaemia	Additional description: Hyperkalaemia		

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	1 x 10E9 pfu	Safety population	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	14 / 15 (93.33%)	
Vascular disorders			
Hypertension	Additional description: Hypertension		
subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	6 / 6 (100.00%)	8 / 15 (53.33%)	
occurrences (all)	9	11	
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	3 / 6 (50.00%)	7 / 15 (46.67%)	
occurrences (all)	3	8	
Chills	Additional description: Chills		
subjects affected / exposed	3 / 6 (50.00%)	3 / 15 (20.00%)	
occurrences (all)	4	4	
Chest discomfort	Additional description: Chest discomfort		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Asthenia	Additional description: Asthenia		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Dyspnoea subjects affected / exposed occurrences (all)	Additional description: Dyspnoea		
	0 / 6 (0.00%)	1 / 15 (6.67%)	
	0	2	
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	Additional description: Depression		
	0 / 6 (0.00%)	1 / 15 (6.67%)	
	0	1	
	Additional description: Anxiety		
	1 / 6 (16.67%)	2 / 15 (13.33%)	
	1	2	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Amylase increased subjects affected / exposed occurrences (all) Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood bicarbonate increased subjects affected / exposed occurrences (all) Transaminases increased subjects affected / exposed occurrences (all) Mean cell volume abnormal subjects affected / exposed occurrences (all) Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) C-reactive protein increased	Additional description: Alanine aminotransferase increased		
	1 / 6 (16.67%)	1 / 15 (6.67%)	
	1	1	
	Additional description: Amylase increased		
	1 / 6 (16.67%)	1 / 15 (6.67%)	
	1	1	
	Additional description: Blood alkaline phosphatase increased		
	1 / 6 (16.67%)	1 / 15 (6.67%)	
	1	1	
	Additional description: Aspartate aminotransferase increased		
	2 / 6 (33.33%)	3 / 15 (20.00%)	
	2	3	
	Additional description: Blood bicarbonate increased		
	0 / 6 (0.00%)	1 / 15 (6.67%)	
	0	1	
	Additional description: Transaminases increased		
	0 / 6 (0.00%)	1 / 15 (6.67%)	
	0	1	
	Additional description: Mean cell volume abnormal		
	0 / 6 (0.00%)	1 / 15 (6.67%)	
	0	1	
	Additional description: Gamma-glutamyltransferase increased		
	1 / 6 (16.67%)	1 / 15 (6.67%)	
	1	1	
	Additional description: C-reactive protein increased		

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Blood creatine phosphokinase increased	Additional description: Blood creatine phosphokinase increased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache	Additional description: Headache		
subjects affected / exposed	2 / 6 (33.33%)	4 / 15 (26.67%)	
occurrences (all)	2	8	
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	0 / 6 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	7	
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	
occurrences (all)	2	5	
Frequent bowel movements	Additional description: Frequent bowel movements		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	1 / 6 (16.67%)	4 / 15 (26.67%)	
occurrences (all)	1	4	
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Abdominal pain upper	Additional description: Abdominal pain upper		

subjects affected / exposed	1 / 6 (16.67%)	3 / 15 (20.00%)	
occurrences (all)	1	3	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	2 / 6 (33.33%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Hepatobiliary disorders			
Hepatic pain	Additional description: Hepatic pain		
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	1 / 6 (16.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Night sweats	Additional description: Night sweats		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Back pain	Additional description: Back pain		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Myalgia	Additional description: Myalgia		
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Infections and infestations			
Cystitis	Additional description: Cystitis		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Hypokalaemia	Additional description: Hypokalaemia		

subjects affected / exposed	0 / 6 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	0 / 6 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	1 / 6 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2019	Protocol version 2.0 dated 14-May-2019: addition of dermatological examination.
24 September 2020	Protocol version 3.0 dated 24-Sep-2020 : addition of 2 dose limiting toxicities, addition of TPOXX as rescue medication, addition of the collection of the history of smallpox vaccination and race/ethnicity data, modification of some inclusion criteria (excluding the patients at risk of hypertensive peaks, and correcting the hemoglobin limit), and addition of other EU countries.
16 December 2020	Protocol version 4.0 dated 16-Dec-2020: modification of some inclusion criteria (clarifying the absence of therapeutic alternatives and the standard anti-cancer treatment, modifying total bilirubin limit, adding alkaline phosphatase limit), addition of exclusion criteria (related to other malignancies, prior gene therapy, history of several reaction to smallpox vaccination, and specifying a visit with the cardiologist), and clarification some concomitant medication restrictions.
18 January 2021	Protocol version 5.0 dated 18-Jan-2021: update the study calendar and specify an exclusion criterion excluding protected adult.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 February 2023	The trial was prematurely terminated per Sponsor decision on 23 February 2023 after the completion of the phase I portion and before the commencement of the phase II, for reasons other than safety.	-

Notes:

Limitations and caveats

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

None reported.

Notes: