Clinical trial results:
A Phase I/II Trial of TG01 and Gemcitabine as Adjuvant Therapy for Treating Patients with Resected Adenocarcinoma of the Pancreas

Summary

EudraCT number	2012-002400-40
Trial protocol	NO GB ES
Global end of trial date	10 May 2019

Results information

Result version number	v1 (current)
This version publication date	22 May 2020
First version publication date	22 May 2020

Trial information

Trial identification

Sponsor protocol code	CT TG01-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02261714
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Targovax ASA
Sponsor organisation address	Lilleakerveien 2C, 0283 Oslo, Norway,
Public contact	Chief Medical Officer, Targovax ASA, +47 213 98 810, contact@targovax.com
Scientific contact	Chief Medical Officer, Targovax ASA, +47 213 98 810, contact@targovax.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	10 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of Phase I of this study was to assess the safety and immune response of co-administration of TG01 with granulocyte macrophage colony stimulating factor (GM-CSF) vaccination when administered concomitantly with adjuvant chemotherapy after primary resection of adenocarcinoma of the pancreas. The objective of Phase II of the study was to further assess the safety, and immune response and efficacy of the TG01/GM-CSF vaccination and adjuvant chemotherapy after primary resection of adenocarcinoma of the pancreas.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki (July 1999), in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (Committee for Proprietary Medicinal Products/ICH/135/95; July 1996), and all applicable regulatory requirements in the countries of conduct.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 January 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 11
Country: Number of subjects enrolled	United Kingdom: 21
Worldwide total number of subjects	32
EEA total number of subjects	32

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	17
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants had confirmed diagnosis of Stage I or II adenocarcinoma of the pancreas, successful surgical resection (R0 or R1), expected to receive gemcitabine as adjuvant chemotherapy ≥12 weeks of surgery, acceptable laboratory test results, Eastern Cooperative Oncology Group performance status of 0 or 1, and a life expectancy of ≥6 months.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Main Group

Arm description:

GM-CSF 0.03 mg & TG01 0.70 mg were given on Days 1 (1 to 12 weeks after surgery), 3, 5, 8, 15 & 22, then every 2 weeks until the end of chemotherapy. If no chemotherapy was started, participants received TG01/GM-CSF on Days 1, 3, 5, 8, 15, 22, 36, 50, & 64, then every 4 weeks until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. When applicable, chemotherapy started at least 3 weeks after initiation of TG01/GM-CSF on Day 22, 36 or 50 of the initial treatment period. Gemcitabine 1000 mg/m^2 was administered intravenously (iv) over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-fluorouracil (5-FU)/leucovorin. Leucovorin was given prior to 5-FU as 60mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	TG01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

TG01 is a sterile lyophilisate consisting of a mixture of 7 peptides. The finished product is a white powder for injection, consisting only of the active substances containing 2.1 mg of peptides (individual peptides comprising 0.3 mg each). The 0.70 mg dose of TG01 was prepared by reconstituting the lyophilisate with sterile water (0.3 mL) for intrdermal injection (0.10 mL injection of a TG01 solution at 7 mg/mL) into the back of the upper arm. The solution was to be used within 6 hours after reconstitution.

Investigational medicinal product name	GM-CSF
Investigational medicinal product code	
Other name	Granulocyte macrophage colony stimulating factor
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

GM-CSF was provided as a lyophilised powder containing 0.1 mg of active substance for reconstitution in sterile water (0.33 mL) for intradermal injection (0.10 mL injection of a GM-CSF solution at 0.3 mg/mL) into the back of the upper arm. GM-CSF was to be administered 10 to 15 minutes before TG01. The solution was to be used within 6 hours after reconstitution.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was provided as a lyophilised powder (vials of 200 mg and 1 g) for reconstitution in saline to be given via iv infusion at a dose of 1000 mg/m^2 over 30 minutes.

Investigational medicinal product name	5-FU
Investigational medicinal product code	
Other name	5-fluorouracil
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

5-FU was provided as a solution for iv injection (vials of 500 mg in 10 mL) administered at a dose of 500 mg/m^2.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin was provided as a solution for iv injection (10 mg/mL) administered at a dose of 60 mg/m^2 or 100 mg.

Arm title	Concomitant Group

Arm description:

GM-CSF 0.03 mg & TG01 0.70 mg was given on Days 1 (9 to 12 weeks after surgery), 3, 5, 8 & 15, then every 2 weeks until the end of chemotherapy. If no chemotherapy was started, participants received TG01/GM-CSF on Days 1, 3, 5, 8, 15, 22, 36, 50, & 64, then every 4 weeks until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. Chemotherapy could start at the same time as TG01/GM-CSF treatment between 9 and 12 weeks after surgery but no later than 12 weeks from the date of surgery. Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	TG01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

TG01 is a sterile lyophilisate consisting of a mixture of 7 peptides. The finished product is a white powder for injection, consisting only of the active substances containing 2.1 mg of peptides (individual peptides comprising 0.3 mg each). The 0.70 mg dose of TG01 was prepared by reconstituting the lyophilisate with sterile water (0.3 mL) for intrdermal injection (0.10 mL injection of a TG01 solution at 7 mg/mL) into the back of the upper arm. The solution was to be used within 6 hours after reconstitution.

Investigational medicinal product name	GM-CSF
Investigational medicinal product code	
Other name	Granulocyte macrophage colony stimulating factor
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

GM-CSF was provided as a lyophilised powder containing 0.1 mg of active substance for reconstitution in sterile water (0.33 mL) for intradermal injection (0.10 mL injection of a GM-CSF solution at 0.3 mg/mL) into the back of the upper arm. GM-CSF was to be administered 10 to 15 minutes before TG01. The solution was to be used within 6 hours after reconstitution.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was provided as a lyophilised powder (vials of 200 mg and 1 g) for reconstitution in saline to be given via iv infusion at a dose of 1000 mg/m^2 over 30 minutes.

Investigational medicinal product name	5-FU
Investigational medicinal product code	
Other name	5-fluorouracil
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

5-FU was provided as a solution for iv injection (vials of 500 mg in 10 mL) administered at a dose of 500 mg/m^2.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin was provided as a solution for iv injection (10 mg/mL) administered at a dose of 60 mg/m^2 or 100 mg.

Arm title	Modified Vaccination Group

Arm description:

GM-CSF 0.03 mg & TG01 0.70 mg were given on Days 1, 8, 15, 22 & 36, then restarted 4 weeks after the end of chemotherapy. If chemotherapy started after Week 10 or not at all, participants received TG01/GM-CSF every 4 weeks from Week 10 until chemotherapy started or until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks (plus once at Week 5 post-chemotherapy) until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. Chemotherapy preferably started at least 3 weeks after initiation of TG01/GM-CSF on Day 22, 36 or 50 of the initial treatment period. Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Arm type	Experimental
Investigational medicinal product name	TG01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

TG01 is a sterile lyophilisate consisting of a mixture of 7 peptides. The finished product is a white powder for injection, consisting only of the active substances containing 2.1 mg of peptides (individual peptides comprising 0.3 mg each). The 0.70 mg dose of TG01 was prepared by reconstituting the lyophilisate with sterile water (0.3 mL) for intrdermal injection (0.10 mL injection of a TG01 solution at 7 mg/mL) into the back of the upper arm. The solution was to be used within 6 hours after reconstitution.

Investigational medicinal product name	GM-CSF
Investigational medicinal product code	
Other name	Granulocyte macrophage colony stimulating factor
Pharmaceutical forms	Solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

GM-CSF was provided as a lyophilised powder containing 0.1 mg of active substance for reconstitution in

sterile water (0.33 mL) for intradermal injection (0.10 mL injection of a GM-CSF solution at 0.3 mg/mL) into the back of the upper arm. GM-CSF was to be administered 15 to 20 minutes before TG01. The solution was to be used within 6 hours after reconstitution.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was provided as a lyophilised powder (vials of 200 mg and 1 g) for reconstitution in saline to be given via iv infusion at a dose of 1000 mg/m^2 over 30 minutes.

Investigational medicinal product name	5-FU
Investigational medicinal product code	
Other name	5-fluorouracil
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

5-FU was provided as a solution for iv injection (vials of 500 mg in 10 mL) administered at a dose of 500 mg/m^2.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin was provided as a solution for iv injection (10 mg/mL) administered at a dose of 60 mg/m^2 or 100 mg.

Number of subjects in period 1	Main Group	Concomitant Group	Modified Vaccination Group
Started	15	4	13
Completed	0	1	3
Not completed	15	3	10
Consent withdrawn by subject	3	-	1
Physician decision	2	-	-
Disease recurrence requiring alternative treatment	5	2	7
Death	2	-	-
Adverse event	3	1	1
Unspecified	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	32	32	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	64.1		
standard deviation	± 8.90	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	21	21	

End points

End points reporting groups

Reporting group title	Main Group

Reporting group description:

GM-CSF 0.03 mg & TG01 0.70 mg were given on Days 1 (1 to 12 weeks after surgery), 3, 5, 8, 15 & 22, then every 2 weeks until the end of chemotherapy. If no chemotherapy was started, participants received TG01/GM-CSF on Days 1, 3, 5, 8, 15, 22, 36, 50, & 64, then every 4 weeks until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. When applicable, chemotherapy started at least 3 weeks after initiation of TG01/GM-CSF on Day 22, 36 or 50 of the initial treatment period. Gemcitabine 1000 mg/m^2 was administered intravenously (iv) over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-fluorouracil (5-FU)/leucovorin. Leucovorin was given prior to 5-FU as 60mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Reporting group title	Concomitant Group

Reporting group description:

GM-CSF 0.03 mg & TG01 0.70 mg was given on Days 1 (9 to 12 weeks after surgery), 3, 5, 8 & 15, then every 2 weeks until the end of chemotherapy. If no chemotherapy was started, participants received TG01/GM-CSF on Days 1, 3, 5, 8, 15, 22, 36, 50, & 64, then every 4 weeks until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. Chemotherapy could start at the same time as TG01/GM-CSF treatment between 9 and 12 weeks after surgery but no later than 12 weeks from the date of surgery. Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Reporting group title	Modified Vaccination Group

Reporting group description:

GM-CSF 0.03 mg & TG01 0.70 mg were given on Days 1, 8, 15, 22 & 36, then restarted 4 weeks after the end of chemotherapy. If chemotherapy started after Week 10 or not at all, participants received TG01/GM-CSF every 4 weeks from Week 10 until chemotherapy started or until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks (plus once at Week 5 post-chemotherapy) until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. Chemotherapy preferably started at least 3 weeks after initiation of TG01/GM-CSF on Day 22, 36 or 50 of the initial treatment period. Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Subject analysis set title	Main + Concomitant Group
Subject analysis set type	Full analysis

Subject analysis set description:

GM-CSF 0.03 mg & TG01 0.70 mg were given on Days 1 (1 to 12 weeks after surgery), 3, 5, 8, 15 & 22 (main group only), then every 2 weeks until the end of chemotherapy. If no chemotherapy was started, participants received TG01/GM-CSF on Days 1, 3, 5, 8, 15, 22, 36, 50, & 64, then every 4 weeks until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. When applicable, chemotherapy started at least 3 weeks after initiation of TG01/GM-CSF (main group) or at the same time (concomitant group). Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Primary: Participants with a Positive Immune Response Assessed by Delayed-type Hypersensitivity (DTH) and/or T-cell Tests

End point title	Participants with a Positive Immune Response Assessed by Delayed-type Hypersensitivity (DTH) and/or T-cell Tests[1][2]

End point description:

An immune responder was defined as a participant who had a positive DTH and/or a positive T-cell test from blood samples collected at least once during the entire study period. The DTH skin reaction

assessment was performed 48 hours (±4 hours) after each administration. The DTH test was considered positive if the area of the skin reaction had an average diameter of ≥5 mm at the 48 hours (±4 hours) assessment. Blood samples were analysed for TG01-specific T-cell responses by proliferation assays. Specific T-cell responses were considered positive if the stimulation index (SI) was ≥2. The SI was derived as mean (T cells + peripheral blood mononuclear cell [PBMC] + TG01)/ mean (T cells + PBMC [negative control]).

End point type	Primary

End point timeframe:

Immune response during the entire study period.

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 formal statistical analyses were planned for the primary endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As participants in the Main Group and Concomitant Group followed similar treatment regimens, the data from these participants was combined and reported in the Main + Concomitant Group.

End point values	Modified Vaccination Group	Main + Concomitant Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	13	19		
Units: Number of participants	12	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Free Survival (DFS) from Surgery Until First Documented Disease Recurrence or Death

End point title	Disease Free Survival (DFS) from Surgery Until First Documented Disease Recurrence or Death[3]

End point description:

DFS at 2 years was defined as the number of months from surgery until first documented disease recurrence or death from any cause. If disease recurrence or death was not recorded for a participant before the end of the study, DFS was censored at the date that they were last known to be recurrence free. If a participant had no post-surgery disease assessment, then DFS was censored at the date of surgery.

9999 = not calculable

End point type	Secondary

End point timeframe:

2 years

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As participants in the Main Group and Concomitant Group followed similar treatment regimens, the data from these participants was combined and reported in the Main + Concomitant Group.

End point values	Modified Vaccination Group	Main + Concomitant Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	13	19		
Units: Months				
median (confidence interval 95%)	19.5 (9.7 to 9999)	13.9 (5.4 to 21.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) from Surgery Until Death

End point title	Overall Survival (OS) from Surgery Until Death[4]

End point description:

OS was defined as the number of months from surgery to death from any cause. If an event (death) was not recorded for a participant before the end of the follow-up, OS was censored at the date that they were last known to be alive.

End point type	Secondary

End point timeframe:

End of follow-up

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As participants in the Main Group and Concomitant Group followed similar treatment regimens, the data from these participants was combined and reported in the Main + Concomitant Group.

End point values	Modified Vaccination Group	Main + Concomitant Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	13	19		
Units: Months				
median (confidence interval 95%)	34.3 (19.2 to 42.5)	33.1 (16.8 to 45.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were to be reported throughout the study and during the 28-day follow-up period after the last administration of study treatment.

Adverse event reporting additional description:

AEs considered related to treatment could have been assessed by the Investigator as causally related to TG01, TG01 only, GM-CSF, GM-CSF only, TG01 and/or GM-CSF, TG01 and GM-CSF only, or chemotherapy only.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Main Group

Reporting group description:

GM-CSF 0.03 mg & TG01 0.70 mg were given on Days 1 (1 to 12 weeks after surgery), 3, 5, 8, 15 & 22, then every 2 weeks until the end of chemotherapy. If no chemotherapy was started, participants received TG01/GM-CSF on Days 1, 3, 5, 8, 15, 22, 36, 50, & 64, then every 4 weeks until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. When applicable, chemotherapy started at least 3 weeks after initiation of TG01/GM-CSF on Day 22, 36 or 50 of the initial treatment period. Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Reporting group title	Concomitant Group

Reporting group description:

GM-CSF 0.03 mg & TG01 0.70 mg was given on Days 1 (9 to 12 weeks after surgery), 3, 5, 8 & 15, then every 2 weeks until the end of chemotherapy. If no chemotherapy was started, participants received TG01/GM-CSF on Days 1, 3, 5, 8, 15, 22, 36, 50, & 64, then every 4 weeks until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. Chemotherapy could start at the same time as TG01/GM-CSF treatment between 9 and 12 weeks after surgery but no later than 12 weeks from the date of surgery. Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Reporting group title	Modified Vaccination Group

Reporting group description:

GM-CSF 0.03 mg & TG01 0.70 mg were given on Days 1, 8, 15, 22 & 36, then restarted 4 weeks after the end of chemotherapy. If chemotherapy started after Week 10 or not at all, participants received TG01/GM-CSF every 4 weeks from Week 10 until chemotherapy started or until Week 52. All participants could then receive TG01/GM-CSF every 4 weeks (plus once at Week 5 post-chemotherapy) until Week 52, then every 12 weeks for up to 2 years or until withdrawal of consent or toxicity. Chemotherapy preferably started at least 3 weeks after initiation of TG01/GM-CSF on Day 22, 36 or 50 of the initial treatment period. Gemcitabine 1000 mg/m^2 was administered iv over 30 minutes on Days 1, 8 & 15 of a 4-week cycle for 6 cycles. Gemcitabine could be substituted with 5-FU/leucovorin. Leucovorin was given prior to 5-FU as 60 mg/m^2 or 100 mg iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles. 5-FU was given as 500 mg/m^2 iv on Days 1 & 2 every 2 weeks of a 4-week cycle for 6 cycles.

Serious adverse events	Main Group	Concomitant Group	Modified Vaccination Group
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 15 (33.33%)	2 / 4 (50.00%)	4 / 13 (30.77%)
number of deaths (all causes)	12	2	4
number of deaths resulting from adverse events	1	0	0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic shock			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			

subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lung infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Biliary sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Main Group	Concomitant Group	Modified Vaccination Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	4 / 4 (100.00%)	13 / 13 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Skin papilloma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	4 / 13 (30.77%)
occurrences (all)	5	1	4
Phlebitis			

subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Peripheral coldness			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Thrombophlebitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	5
Surgical and medical procedures			
Skin neoplasm excision			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 15 (53.33%)	4 / 4 (100.00%)	10 / 13 (76.92%)
occurrences (all)	11	6	16
Influenza like illness			
subjects affected / exposed	4 / 15 (26.67%)	3 / 4 (75.00%)	2 / 13 (15.38%)
occurrences (all)	7	7	4
Pyrexia			
subjects affected / exposed	5 / 15 (33.33%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	8	1	0
Injection site reaction			
subjects affected / exposed	4 / 15 (26.67%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	7	1	0
Chills			

subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	4 / 13 (30.77%)
occurrences (all)	1	1	5
Injection site pruritus			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	2 / 13 (15.38%)
occurrences (all)	2	1	9
Oedema peripheral			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	2 / 13 (15.38%)
occurrences (all)	2	1	3
Injection site erythema			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	4	0	3
Mucosal inflammation			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Feeling hot			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Injection site swelling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Vaccination site pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Vaccination site reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Injection site bruising			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Injection site urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Vaccination site pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Cellulitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	2
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Biliary sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Anaphylactic reaction			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Allergy to vaccine			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Anaphylactic shock			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	2 / 13 (15.38%)
occurrences (all)	2	1	4
Dyspnoea exertional			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Pulmonary embolism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Productive cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Haemoptysis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Orthopnoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Rhinorrhoea			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 15 (26.67%)	1 / 4 (25.00%)	6 / 13 (46.15%)
occurrences (all)	4	1	6
Anxiety			
subjects affected / exposed	2 / 15 (13.33%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	2	1	1
Depressed mood			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	3 / 15 (20.00%)	2 / 4 (50.00%)	2 / 13 (15.38%)
occurrences (all)	4	4	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood glucose fluctuation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Platelet count increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Vitamin D decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Ligament sprain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Abdominal wound dehiscence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Alcohol poisoning			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Femoral neck fracture			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Incisional hernia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Inflammation of wound			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 15 (13.33%)	3 / 4 (75.00%)	3 / 13 (23.08%)
occurrences (all)	4	3	5
Dysgeusia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	3	0	1
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	3 / 13 (23.08%)
occurrences (all)	2	0	3
Paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3
Hyperaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Sciatica			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Cognitive disorder			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Coordination abnormal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Transient ischaemic attack			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	5 / 15 (33.33%)	2 / 4 (50.00%)	7 / 13 (53.85%)
occurrences (all)	7	2	13
Anaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Thrombocytopenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	2
Eye disorders			
Eyelid oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Eye pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Foreign body sensation in eyes			

subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Diplopia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Eye haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 15 (46.67%)	2 / 4 (50.00%)	7 / 13 (53.85%)
occurrences (all)	10	2	10
Nausea			
subjects affected / exposed	8 / 15 (53.33%)	1 / 4 (25.00%)	7 / 13 (53.85%)
occurrences (all)	32	1	10
Diarrhoea			
subjects affected / exposed	5 / 15 (33.33%)	2 / 4 (50.00%)	5 / 13 (38.46%)
occurrences (all)	5	2	6
Vomiting			
subjects affected / exposed	4 / 15 (26.67%)	1 / 4 (25.00%)	6 / 13 (46.15%)
occurrences (all)	13	1	7
Abdominal pain upper			
subjects affected / exposed	2 / 15 (13.33%)	2 / 4 (50.00%)	1 / 13 (7.69%)
occurrences (all)	2	2	1
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	2 / 4 (50.00%)	0 / 13 (0.00%)
occurrences (all)	1	2	0
Mouth ulceration			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0

Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Flatulence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Abdominal distension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Abdominal pain lower			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Abdominal hernia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Glossodynia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Steatorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Faeces pale			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Dry skin			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Pruritus			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	3	0	1
Rash			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	1	1	2
Night sweats			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	3 / 13 (23.08%)
occurrences (all)	0	0	3
Diabetic foot			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Rash maculo-papular			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cold sweat			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Scar pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			

subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Renal ischaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	3 / 13 (23.08%)
occurrences (all)	2	0	3
Joint swelling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	2
Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Back pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	2
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3
Musculoskeletal chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Limb mass			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Arthritis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Bone pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Pneumonia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Tooth infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	4
Tooth abscess			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3
Abdominal wall abscess			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0
Abscess of eyelid			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Angular cheilitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Infected bite			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Labyrinthitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Lung infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0
Urosepsis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 15 (33.33%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	5	0	1
Hyperglycaemia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	3	0	1
Diabetes mellitus			
subjects affected / exposed	1 / 15 (6.67%)	1 / 4 (25.00%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Gout			

subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 4 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 4 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2013	Amendments 1.0 (dated 22 March 2013) and 1.1 and (dated 12 April 2013) included the following: • Participants were not to be replaced if they discontinued due to disease recurrence. • The requirement to administer gemcitabine 1 hour after TG01 administration was relaxed to allow gemcitabine to be administered on the same day but after TG01. • After completion of gemcitabine treatment, the requirement for participants to discontinue TG01/GM-CSF treatment if they received alternative therapy for pancreatic cancer was removed. • Inclusion criterion for haemoglobin levels was changed from ≥10 g/dL to ≥9 g/dL. • Inclusion criterion for creatinine clearance ≥60 mL/min was changed to a requirement for serum creatinine ≤1.5x upper normal limit (UNL). • Timings for DTH skin test injections and laboratory test evaluations clarified in text. • The requirement to discontinue TG01/GM-CSF if gemcitabine was discontinued was removed. • Addition of collection of a sample for assessment of T-cell response at Week 52. • Removal of assessment for DTH response at end of treatment.
20 May 2013	Amendment 2.0 (dated 20 May 2013) included the following: • Increase to maximum number of centres from 2 to 3. • Additional objectives added: To monitor CA19-9 and other biomarker levels. Details added for collection of blood samples and analysis for these endpoints. • Additional inclusion criteria added requiring participants to be expected to receive gemcitabine as adjuvant chemotherapy and for AST/ALT levels to be ≤5xUNL. • Changes to exclusion criteria: participants were not to be excluded if they had experienced significant weight loss before surgery (≥10% weight loss) but were to be excluded if they were unlikely to start chemotherapy within 12 weeks of surgery and/or were not expected to receive 6 cycles of chemotherapy. • Addition of 5-FU/leucovorin as optional adjuvant chemotherapy. • Clarification that chemotherapy was to start no less than 3 weeks after the start of TG01/GM-CSF but no later than 12 weeks after surgery. • Clarification that 6 cycles of chemotherapy were to be administered. • Additional details of assessments added.
24 June 2013	Amendment 3.0 (dated 24 June 2013) included the following: • Further to addition of 5-FU/leucovorin as optional adjuvant chemotherapy in Amendment 2.0, references to assessments of effects of 'gemcitabine' updated to 'chemotherapy'. • Analysis populations updated.

17 July 2013	Amendments 4.0 (dated 17 July 2013) and 4.1 (dated 25 September 2013) included the following: • Increase in the maximum number of centres from 3 to 4 and locations specified as Norway and UK. • Secondary objective regarding assessment of safety of TG01/GM-CSF vaccination and adjuvant chemotherapy updated to a primary objective and additional details of endpoints for safety added. • Primary objective regarding assessment of immune response clarified. • Secondary objective of clinical efficacy to be assessed at 2 years. • Exploratory objective regarding Kirsten rat sarcoma viral oncogene homolog status clarified. • Treatment with TG01/GM-CSF to start within 1 to 8 weeks after surgery in Phase I part of the study. • Details of schedule for TG01/GM-CSF treatment after completion of chemotherapy treatment updated and participants who did recur but had a positive immune response during the initial treatment period allowed to continue TG01/GM-CSF treatment. • Criteria regarding granulocyte count for continuation of gemcitabine treatment updated. • Clarification that computed tomography scans should be performed after surgery, every 6 months from start of vaccination and at any time point if indicated although not mandatory. • Details regarding nominated data management group added. • Additional exclusion criteria added excluding participants who planned to receive yellow fever or other live (attenuated) vaccine during the course of the study. • Clarification of SAE reporting timelines.
30 April 2014	Amendments 5.0, 5.1, and 5.2 (dated 30 April 2014, 06 June 2014, and 04 July 2014 respectively) included the following: • Sponsor name updated from Aptiv Solutions to Targovax AS; contact details updated for Sponsor personnel. • Duration of enrolment and overall study duration updated. • Primary objective and endpoint clarified. • Number of blood samples and total volume of blood collected updated. • Number of participants planned for the Phase II part of the study increased from 12-18 to 18-24 with a maximum of 6 participants in the Concomitant Group. • Clarification of assessments for Main Group. • Addition of criteria for inclusion of participants in a Concomitant Group. • Addition of details of assessments and treatment for participants included in the Concomitant Group and for participants who do not start chemotherapy at all including treatment schedule and schedule of visits. • A survival follow-up added for participants who discontinued before 2 years. • Definition of 'successful surgical resection' updated in inclusion criteria. • Clarification of storage conditions after reconstitution of TG01 and GM-CSF. • Assessment of immune response for Concomitant Group added. • Assessment of immune response, CA19-9 levels and levels of other biomarkers at Week 52 and end of study added. • Definitions of analysis populations updated. • Clarification that events that were unequivocally due to disease recurrence were not to be reported as AEs and clarification of when laboratory/vital signs abnormalities should be considered AEs.
28 January 2015	Amendment 6.0 (dated 28 January 2015) included the following: • Inclusion of prophylactic treatment prior to TG01/GM-CSF administrations after the end of chemotherapy. • Requirement for participants to be observed for 30 minutes after each injection of TG01. • Requirement for the DTH TG01 injection to be given 30 minutes before administration of GM-CSF. • Addition of treatment schedule for participants starting vaccination treatment but receiving chemotherapy later. • Updated details for Sponsor and for Safety Reporting. • Anticipated toxicity and management details updated.

12 March 2015	Amendment 7.0 (dated 12 March 2015) included the following: • Number of trial centres updated and locations of centres updated to include Spain. • Addition of a new cohort of up to 13 participants (Modified Vaccination Group) to the Phase II part of the study increasing total study duration to 5 years. Addition of all details regarding treatment and assessments for this additional group of participants. • Clarified participants who would constitute the Main Group and the Concomitant Group. • Pre-medication with intravenous anti-histamine treatment added for any participants who exhibited signs of an allergic reaction for all subsequent TG01 administrations. • Definition of acceptable immune response clarified.
27 June 2016	Amendment 8.0 (dated 27 June 2016) included the following: • Sponsor details updated. • Extension of study to include survival follow-up assessments until last participant last visit in the Modified Vaccination Group. • Number of blood samples and total volume of blood collected updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported