Clinical trial results:
A Double-blind, Placebo-controlled, Randomized, Phase 2 Study to Evaluate the Efficacy and Safety of Maintenance Therapy With PankoMab-GEX™ After Chemotherapy in Patients With Recurrent Epithelial Ovarian Carcinoma

Summary

EudraCT number	2013-000931-28
Trial protocol	IT DE HU ES GB PL
Global end of trial date	28 July 2017

Results information

Result version number	v1 (current)
This version publication date	16 December 2020
First version publication date	16 December 2020

Trial information

Trial identification

Sponsor protocol code	GEXMab25201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01899599
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Glycotope GmbH
Sponsor organisation address	Robert Roessle St 10, Berlin, Germany, 13125
Public contact	Reception desk, Glycotope GmbH, +49 3094892600, Trials@glycotope.com
Scientific contact	Reception desk, Glycotope GmbH, +49 3094892600, Trials@glycotope.com
Sponsor organisation name	Glycotope GmbH
Sponsor organisation address	Robert-Rössle-Str. 10, Berlin, Germany, 13125
Public contact	Isabelle Ahrens-Fath, PhD, Glycotope GmbH, +49 3094892600, isabelle.ahrens-fath@glycotope.com
Scientific contact	Isabelle Ahrens-Fath, PhD, Glycotope GmbH, +49 3094892600, isabelle.ahrens-fath@glycotope.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	08 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 April 2017
Global end of trial reached?	Yes
Global end of trial date	28 July 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary study objective is:
To evaluate the efficacy of maintenance therapy with single-agent PankoMab-GEX™ compared to placebo as assessed by progression free survival (PFS) following chemotherapy in patients with recurrent epithelial ovarian carcinoma.

Protection of trial subjects:

The protocol (and any amendments) and the statement of informed consent were approved by an independent ethics committee (IEC) prior to each center's Initiation.
The study was conducted in accordance with the Declaration of Helsinki and its revisions as well as with the valid national law(s) of the participating country/ies, with the International Conference on Harmonisation (ICH) Harmonised Tripartite Guideline for Good Clinical Practice (GCP) (E6) issued in July 1996, and with the Directive 2001/20/EC and Regulation EU No 536/2014. Each investigator conducted the study according to applicable local or regional regulatory requirements and applicable national regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 July 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Italy: 37
Country: Number of subjects enrolled	Russian Federation: 35
Country: Number of subjects enrolled	Romania: 22
Worldwide total number of subjects	216
EEA total number of subjects	181

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)	131
From 65 to 84 years	84
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

At Pre-screening, the general eligibility of the patients for study participation was assessed by confirmation of TA-MUC 1 +, recurrent epithelial ovarian or fallopian-tube cancer, or primary peritoneal cancer with high-grade (Grade 2 or 3) serous features or a serous component.

Pre-assignment

Screening details:

Patients had to have recurrent epithelial primary ovarian, fallopian tube, or high grade primary peritoneal cancer, immune-histologically confirmed as TA-MUC1-positive (immuno-reactive score [IRS] ≥3). Patients had to have received at least 2 lines but not more than 5 lines of chemotherapy prior to the start of maintenance treatment.

Pre-assignment period milestones

Number of subjects started	216
Number of subjects completed	216

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

Patients who met all of the eligibility criteria for the study were randomized by centralized IWRS in a 2:1-ratio to receive either PankoMab-GEX™ or placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pankomab-GEX

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Pankomab-GEX
Investigational medicinal product code	
Other name	Gatipotuzumab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received a starting dose of 500 mg PankoMab-GEX™ on Day 1 of the study (start of Cycle 0). Thereafter, PankoMab-GEX™ (1700 mg) was administered on the first day of each 3-week treatment cycle, starting on Day 8 after randomization (start of Cycle 1). Patients continued to receive treatment with a 3-week interval (q3w) ± 3 days until disease progression (according modified RECIST V1.1 irRC; i.e. increase of CA125 alone was no criterion for disease progression) or until they exhibited any discontinuation criteria.

Arm title	Placebo

Arm description: -

Arm type	Placebo

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

Dosage and administration details:

Route of administration: i.v. over 3 hours matching Pankomab-GEX

Number of subjects in period 1	Pankomab-GEX	Placebo
Started	151	65
Completed	133	55
Not completed	18	10
Consent withdrawn by subject	4	3
Adverse event, non-fatal	2	3
not specified	12	2
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Pankomab-GEX
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Pankomab-GEX	Placebo	Total
Number of subjects	151	65	216
Age categorical Units: Subjects			
Adults (18-64 years)	92	40	132
From 65-84 years	58	25	83
85 years and over	1	0	1
Age continuous Units: years			
median	61.0	60.0	
full range (min-max)	34 to 86	29 to 79	-
Gender categorical			
Based on the indication "Ovarian Cancer" only female patients participated in the study			
Units: Subjects			
Female	151	65	216
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Intent-to-treat population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat (ITT) population was defined as all randomized patients - patients were analyzed as randomized.
Three patients were randomized (One patient in the placebo group and two patients in the PankoMab-GEX™ group) but were excluded from the ITT population because of the lack of signature on the consent form.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population was defined as all randomized patients having received IMP at least once

Reporting group values	Intent-to-treat population	Safety population	
Number of subjects	213	212	
Age categorical Units: Subjects			
Adults (18-64 years)	130	129	
From 65-84 years	82	82	
85 years and over	1	1	

Age continuous Units: years			
median	61.0	61.0	
full range (min-max)	29 to 86	29 to 86	
Gender categorical			
Based on the indication "Ovarian Cancer" only female patients participated in the study			
Units: Subjects			
Female	213	212	
Male	0	0	

End points

End points reporting groups

Reporting group title	Pankomab-GEX
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Intent-to-treat population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat (ITT) population was defined as all randomized patients - patients were analyzed as randomized.
Three patients were randomized (One patient in the placebo group and two patients in the PankoMab-GEX™ group) but were excluded from the ITT population because of the lack of signature on the consent form.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population was defined as all randomized patients having received IMP at least once

Primary: Progression free survival

End point title	Progression free survival

End point description:

PFS, as assessed by the site investigator and defined as the time interval from the date of randomization to the first date of documented disease progression using modified irRC based on RECIST, or death due to any cause.

End point type	Primary

End point timeframe:

Time interval from the date of randomization to the first date of documented disease progression using modified irRC based on RECIST version 1.1 , or death due to any cause

End point values	Pankomab-GEX	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	64		
Units: weeks				
median (confidence interval 95%)	15.286 (14.286 to 20.143)	15.000 (13.143 to 20.486)		

Statistical analyses

Statistical analysis title	Cox Proportional Hazards Model
Comparison groups	Pankomab-GEX v Placebo

Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8003
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.959
Confidence interval	
level	95 %
sides	1-sided
lower limit	0.69

Secondary: Progression Free Survival (central asssment)

End point title	Progression Free Survival (central asssment)

End point description:

PFS, as assessed by Independent central review and defined as the time interval from the date of randomization to the first date of documented disease progression using modified irRC based on RECIST, or death due to any cause.

End point type	Secondary

End point timeframe:

Time interval from the date of randomization to the first date of documented disease progression using modified irRC based on RECIST version 1.1 , or death due to any cause

End point values	Pankomab-GEX	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	64		
Units: weeks				
median (confidence interval 95%)	14.14 (8.71 to 14.43)	14.14 (8.57 to 15.29)		

Statistical analyses

Statistical analysis title	Cox proportional Hazards Model
Comparison groups	Pankomab-GEX v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7972
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.047

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.739
upper limit	1.482

Secondary: Progression Free Survival (GCIC criteria)

End point title	Progression Free Survival (GCIC criteria)

End point description:

PFS as assessed according to Gynecologic Cancer Intergroup (GCIG) criteria

End point type	Secondary

End point timeframe:

Time interval from the date of randomization to the first date of documented disease progression or death due to any cause

End point values	Pankomab-GEX	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	64		
Units: weeks				
median (confidence interval 95%)	29.00 (23.71 to 47.14)	22.29 (16.43 to 51.14)		

Statistical analyses

Statistical analysis title	Cox Proportional Hazards Model
Comparison groups	Pankomab-GEX v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1368
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.704
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.443
upper limit	1.118

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:	
The ORR was defined as the combined rate of best response of CR or PR as assessed by investigator	
End point type	Secondary
End point timeframe:	
From randomization until end of treatment	

End point values	Pankomab-GEX	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	64		
Units: Percent				
number (confidence interval 95%)	3.36 (1.10 to 7.66)	6.25 (1.73 to 15.24)		

Statistical analyses

Statistical analysis title	Fisher exact test
Comparison groups	Placebo v Pankomab-GEX
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4573
Method	Fisher exact
Parameter estimate	Mean difference (net)
Point estimate	-2.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.45
upper limit	11.71

Secondary: Clinical Benefit Rate	
End point title	Clinical Benefit Rate
End point description:	
The CBR was defined as Best Overall Response of CR, PR, and SD	
End point type	Secondary
End point timeframe:	
From randomization until end of treatment	

End point values	Pankomab-GEX	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	64		
Units: Percent				
number (confidence interval 95%)	60.40 (52.07 to 68.31)	57.81 (44.82 to 70.06)		

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel
Comparison groups	Pankomab-GEX v Placebo
Number of subjects included in analysis	213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7872
Method	Cochran-Mantel-Haenszel

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From randomization until end of treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	Pankomab-GEX
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Pankomab-GEX	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 149 (9.40%)	8 / 63 (12.70%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	2	
Investigations			
Blood creatine increased			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Seroma			
subjects affected / exposed	0 / 149 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure acute			

subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 149 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periardial effusion			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 149 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 149 (0.67%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 149 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 149 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Device related infection			
subjects affected / exposed	2 / 149 (1.34%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 149 (1.34%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 149 (0.67%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			

subjects affected / exposed	0 / 149 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 149 (0.67%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pankomab-GEX	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 149 (87.25%)	51 / 63 (80.95%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 149 (6.04%)	3 / 63 (4.76%)	
occurrences (all)	10	3	
Flushing			
subjects affected / exposed	9 / 149 (6.04%)	1 / 63 (1.59%)	
occurrences (all)	9	1	
Nervous system disorders			

Headache			
subjects affected / exposed	23 / 149 (15.44%)	9 / 63 (14.29%)	
occurrences (all)	36	9	
Dizziness			
subjects affected / exposed	12 / 149 (8.05%)	2 / 63 (3.17%)	
occurrences (all)	14	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	25 / 149 (16.78%)	6 / 63 (9.52%)	
occurrences (all)	55	6	
Asthenia			
subjects affected / exposed	19 / 149 (12.75%)	8 / 63 (12.70%)	
occurrences (all)	23	9	
Fatigue			
subjects affected / exposed	21 / 149 (14.09%)	5 / 63 (7.94%)	
occurrences (all)	24	6	
Chills			
subjects affected / exposed	8 / 149 (5.37%)	4 / 63 (6.35%)	
occurrences (all)	13	4	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	27 / 149 (18.12%)	13 / 63 (20.63%)	
occurrences (all)	36	17	
Nausea			
subjects affected / exposed	25 / 149 (16.78%)	10 / 63 (15.87%)	
occurrences (all)	46	12	
Vomiting			
subjects affected / exposed	18 / 149 (12.08%)	8 / 63 (12.70%)	
occurrences (all)	24	17	
Diarrhoea			
subjects affected / exposed	17 / 149 (11.41%)	6 / 63 (9.52%)	
occurrences (all)	23	8	
Abdominal pain upper			
subjects affected / exposed	10 / 149 (6.71%)	5 / 63 (7.94%)	
occurrences (all)	7	3	
Constipation			

subjects affected / exposed	11 / 149 (7.38%)	3 / 63 (4.76%)	
occurrences (all)	15	3	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	19 / 149 (12.75%)	3 / 63 (4.76%)	
occurrences (all)	24	3	
Cough			
subjects affected / exposed	12 / 149 (8.05%)	5 / 63 (7.94%)	
occurrences (all)	15	5	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	21 / 149 (14.09%)	4 / 63 (6.35%)	
occurrences (all)	28	4	
Erythema			
subjects affected / exposed	15 / 149 (10.07%)	5 / 63 (7.94%)	
occurrences (all)	20	7	
Rash			
subjects affected / exposed	10 / 149 (6.71%)	2 / 63 (3.17%)	
occurrences (all)	14	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	8 / 149 (5.37%)	4 / 63 (6.35%)	
occurrences (all)	9	5	
Insomnia			
subjects affected / exposed	8 / 149 (5.37%)	3 / 63 (4.76%)	
occurrences (all)	9	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	15 / 149 (10.07%)	4 / 63 (6.35%)	
occurrences (all)	16	20	
Arthralgia			
subjects affected / exposed	11 / 149 (7.38%)	5 / 63 (7.94%)	
occurrences (all)	14	5	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed occurrences (all)	12 / 149 (8.05%) 14	6 / 63 (9.52%) 6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2016	# Addition of disease assessment according to RECIST 1.1 criteria # Introduction of the definition of study termination # Changes in study design: An open label portion was added to the study after the primary analysis in order to collect more robust data for overall survival and safety endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported