

**Clinical trial results:****A Phase 1/2a, Open-Label, Parallel, Two-Arm, Dose-Escalation Study to Assess the Safety, Tolerability, Efficacy, Pharmacokinetics, and Pharmacodynamics of BAX69 in Subjects with Refractory Ovarian Cancer with Malignant Ascites****Summary**

EudraCT number	2015-003492-29
Trial protocol	HU
Global end of trial date	26 May 2016

Results information

Result version number	v1 (current)
This version publication date	08 June 2017
First version publication date	08 June 2017

Trial information**Trial identification**

Sponsor protocol code	391402
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02540356
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Baxalta Innovations GmbH
Sponsor organisation address	Industriestrasse 67, Vienna, Austria, 1221
Public contact	Clinical Trial Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.com
Scientific contact	Clinical Trial Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.com
Sponsor organisation name	Baxalta US Inc.
Sponsor organisation address	One Baxter Way, Westlake Village, United States, CA 91362
Public contact	Clinical Trial Registries and Results Disclosure, Baxalta US Inc., ClinicalTrialsDisclosure@baxalta.com
Scientific contact	Clinical Trial Registries and Results Disclosure, Baxalta US Inc., ClinicalTrialsDisclosure@baxalta.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	26 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2016
Global end of trial reached?	Yes
Global end of trial date	26 May 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the maximum tolerated dose (MTD) and the recommended phase 2 dose (RP2D) of imalumab (BAX69) and to compare puncture-free survival (PuFS) to puncture-free interval at baseline.

Protection of trial subjects:

The study was conducted in accordance with the study protocol, the International Conference on Harmonization Guideline for Good Clinical Practice E6 (ICH GCP April 1996), Title 21 of the US Code of Federal Regulations (US CFR), the European Clinical Trial Directive (2001/20/EC and 2005/28/EC), and applicable national and local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
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 States: 2
Worldwide total number of subjects	2
EEA total number of subjects	0

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)	1
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was stopped early with only 1 subject having been dosed.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	2
Number of subjects completed	1

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 1
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Period 1

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

Arms

Arm title	Single-Route Arm
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Arm description:

Imalumab (BAX69) administered weekly by intraperitoneal (IP) infusion only.

Arm type	Experimental
Investigational medicinal product name	Imalumab
Investigational medicinal product code	BAX69
Other name	BAX69
Pharmaceutical forms	Solution for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

In the Single-Route Arm, Imalumab (BAX69) will be administered intraperitoneal (IP) as 1 of the following predefined dose regimens: 5 mg/kg IP (Cohort S1), 10 mg/kg IP (Cohort S2), 15 mg/kg IP (Cohort S3). IP infusion will be administered at a flowrate of between 6.3 mL/min and 10.0 mL/min.

Number of subjects in period 1^[1]	Single-Route Arm
Started	1
Completed	0
Not completed	1
terminated from study due to disease progression	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 2 subjects provided informed consent and were screened for study participation. One subject was a screen failure and did not enter the baseline period.

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
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Reporting group description:

Imalumab (BAX69) administered weekly by intraperitoneal (IP) infusion.

Reporting group values	Overall Trial	Total	
Number of subjects	1	1	
Age categorical			
Units: Subjects			
From 65-84 years	1	1	
Gender categorical			
Units:			
Male	0	0	
Female	1	1	

End points

End points reporting groups

Reporting group title	Single-Route Arm
Reporting group description: Imalumab (BAX69) administered weekly by intraperitoneal (IP) infusion only.	

Primary: The occurrence of dose-limiting toxicity (DLT)

End point title	The occurrence of dose-limiting toxicity (DLT) ^[1]
End point description: Study was terminated early with only one subject dosed. No statistical analysis performed. DLT is defined as any drug related treatment-emergent adverse event that occurs during the 28-day period after the first dose of Imalumab and that meets any of these criteria: - Any \geq grade 3 non-hematologic toxicity assessed by the investigator as related to study drug (except: single lab value out of normal range not necessarily translating or considered a feature of clinical diagnosis requiring an intervention per investigator's interpretation and resolves to \leq Grade 2 with adequate measure in 7 days; Transient grade 3 elevations of hepatic transaminases in the absence of simultaneous increase in serum bilirubin; Alopecia) - Any toxicity resulted in dose delay for \geq 14 days - Any grade 4 hematologic toxicity (except lymphopenia) - Grade 3 febrile neutropenia - Grade 3 thrombocytopenia associated with bleeding - Any life-threatening complication/abnormality not covered in NCICTCAE v4.03	
End point type	Primary
End point timeframe: 28 days after the first dose of Imalumab	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to early study termination no statistical analysis was performed.

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: The ratio of puncture free survival (PuFS) over puncture-free interval at baseline

End point title	The ratio of puncture free survival (PuFS) over puncture-free interval at baseline ^[2]
End point description: Study was terminated early with only one subject dosed. No statistical analysis was performed. PuFS is defined as the time from the last dose of Imalumab to the first therapeutic paracentesis after that, or death, whichever occurs first. Puncture-free interval at baseline is calculated as the time between the last 2 therapeutic paracenteses immediately before the first dose of Imalumab.	

End point type	Primary
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End point timeframe:

Throughout the study period

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to early study termination no statistical analysis was performed.

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[3]			
Units: Not available				

Notes:

[3] - No statistical analysis performed for this endpoint due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: The ratio of time to first paracentesis post-treatment over puncture-free interval at baseline

End point title	The ratio of time to first paracentesis post-treatment over puncture-free interval at baseline
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End point description:

Study was terminated early with only one subject dosed. No statistical analysis was performed. Time to first paracentesis post-treatment is calculated as the time between the last dose of Imalumab to subsequent first therapeutic paracentesis.

End point type	Secondary
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End point timeframe:

Throughout the study period.

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[4]			
Units: Not available				

Notes:

[4] - No statistical analysis performed for this endpoint due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: The change in ascites volume per unit time with treatment

End point title	The change in ascites volume per unit time with treatment
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End point description:

Study was terminated early with only one subject dosed. No statistical analysis was performed. The volume of ascites from the last dose of Imalumab to the first post-treatment paracentesis per unit time will be compared to the volume of the last pre-treatment paracentesis per unit time. At each paracentesis, the volume of fluid that can be removed safely (measured by ultrasound-guided

paracentesis) to achieve close to dryness should be withdrawn, measured, and documented.

End point type	Secondary
End point timeframe:	
Throughout the study period	

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[5]			
Units: Not available				

Notes:

[5] - No statistical analysis performed for this endpoint due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: The changes in ascites-related symptoms

End point title	The changes in ascites-related symptoms
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End point description:

Study was terminated early with only one subject dosed. No statistical analysis was performed. Ascites related symptoms: anorexia, nausea, early satiety, vomiting, abdominal pain, abdominal swelling, dyspnea, fatigue, swollen ankles, heartburn

End point type	Secondary
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End point timeframe:

Baseline, weekly during the treatment period, and every 2 weeks during the safety follow-up period.

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: Not available				

Notes:

[6] - No statistical analysis performed for this endpoint due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of serious adverse events (SAEs) and/or treatment emergent adverse events (TEAEs), regardless of causality or relationship to study drug

End point title	Occurrence of serious adverse events (SAEs) and/or treatment emergent adverse events (TEAEs), regardless of causality or relationship to study drug
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End point description:

Study was terminated early with only one subject dosed. No statistical analysis was performed.

End point type	Secondary
End point timeframe: Throughout the study period	

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Subjects				
SAEs	0			
TEAEs related to study drug	0			
TEAEs not related to study drug	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of binding and/or neutralizing anti-BAX69 antibodies following treatment with BAX69

End point title	Occurrence of binding and/or neutralizing anti-BAX69 antibodies following treatment with BAX69			
End point description: Study was terminated early with only one subject dosed. No statistical analysis was performed.				
End point type	Secondary			
End point timeframe: Throughout the study period				

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[7]			
Units: Not available				

Notes:

[7] - No statistical analysis performed for this endpoint due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: BAX69 plasma pharmacokinetic (PK) parameters

End point title	BAX69 plasma pharmacokinetic (PK) parameters			
End point description: Study was terminated early with only one subject dosed. No statistical analysis was performed.				

Maximum and minimum observed concentration (C_{max} and C_{min}), Area under the concentration vs time curve (AUC), half-life (t_{1/2}), apparent systemic clearance (CL/F), volume of distribution (V_z/F)

End point type	Secondary
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End point timeframe:

Pre-dose and post-dose at 1.5, 4, 8, 24, and 72 hours

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[8]			
Units: Not available				

Notes:

[8] - No statistical analysis performed for this endpoint due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life (QoL) measure

End point title	Quality of Life (QoL) measure
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End point description:

QoL will be assessed using EORTC QLQ-C30.

Study was terminated early with only one subject dosed. No statistical analysis was performed.

End point type	Secondary
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End point timeframe:

Weekly from the baseline visit to the last week of safety follow-up (8 weeks or longer, if additional treatment will be implemented)

End point values	Single-Route Arm			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[9]			
Units: Not available				

Notes:

[9] - No statistical analysis performed for this endpoint due to early study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of Imalumab until study completion/discontinuation or 56 (\pm 2 days) following the last dose of Imalumab.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Overall Trial
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Reporting group description:

BAX69 administered weekly by intraperitoneal (IP) infusion only.

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Gastrointestinal disorders			
Abdominal distention (Grade 2)			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Right knee pain (Grade 1)			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypokalemia (Grade 1)			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

Hypomagnesemia (Grade 1) subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1		
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2015	Definition of DLT was changed according to FDA recommendation.
14 August 2015	Revision of inclusion criteria for adequate renal function including estimated glomerular filtration rate >50mL/min/1,73m ² . Text added to describe process of preparation and storage of BAX69 for IV and IP infusion. Description of BAX69 administration by IP infusion updated. Multi-gated acquisition scan added. Description of the information to be captured in the Case Report Form for each study drug administration was revised. Clarification regarding events relating to clinical deterioration. New text regarding safety reporting added. Information concerning medical care for AEs during the study added.
30 October 2015	Clarification of safety assessments in subjects receiving maintenance therapy and in those not receiving maintenance therapy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Study was terminated early with only 1 subject having been dosed in the single-route arm. Therefore no statistical analysis was performed for this study. Only descriptive data for one subject are available.

Notes: