



Clinical trial results:

A First-in-human Dose-escalation and Dose-finding Phase 1 Trial of IMAB027 in Patients with Recurrent Advanced Ovarian Cancer

Summary

EudraCT number	2013-002755-15
Trial protocol	BE
Global end of trial date	28 October 2015

Results information

Result version number	v1 (current)
This version publication date	14 March 2019
First version publication date	14 March 2019

Trial information

Trial identification

Sponsor protocol code	GM-IMAB-002-01
-----------------------	----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02054351
WHO universal trial number (UTN)	-
Other trial identifiers	Protocol Number: 1650-CL-0101, Acronym: OVAR

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Global Development US
Sponsor organisation address	1 Astellas Way, Northbrook, IL, United States, 60062
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Development US, astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Development US, astellas.resultsdisclosure@astellas.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	28 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to assess the safety and tolerability of ASP1650 at each dose tested and to define the maximum tolerated dose (MTD) based on dose-limiting toxicity (DLT).

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 February 2014
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	Belgium: 17
Country: Number of subjects enrolled	Germany: 25
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	21

From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an all female study, for participants with recurrent advanced ovarian cancer.

Pre-assignment

Screening details:

Eligible participants who met inclusion criteria and none of the exclusion criteria were enrolled. A total of 43 female participants were enrolled in Stages 1 and 2 of the study. One participant that enrolled in Stage 2, was a screen failure due to an adverse event (AE) experienced before being assigned to a dosing cohort.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ASP1650 Stage 1/2 1-1000 mg/m ²

Arm description:

Stage 1 participants received weekly intrasubject dose escalation of 1 mg/m², 10 mg/m², 30 mg/m² and 100 mg/m² ASP1650. Stage 2 participants received 100 mg/m², 300 mg/m², 600 mg/m² or 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants in lower doses may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Arm type	Experimental
Investigational medicinal product name	ASP1650
Investigational medicinal product code	
Other name	IMAB027
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ASP1650 was given as a 2 hour intravenous (IV) infusion.

Arm title	ASP1650 Stage 2 - 100 mg/m ²
------------------	---

Arm description:

Participants received 100 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Arm type	Experimental
Investigational medicinal product name	ASP1650
Investigational medicinal product code	
Other name	IMAB027
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ASP1650 was given as a 2 hour intravenous (IV) infusion.

Arm title	ASP1650 Stage 2 - 300 mg/m ²
------------------	---

Arm description:

Participants received 300 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Arm type	Experimental
Investigational medicinal product name	ASP1650
Investigational medicinal product code	
Other name	IMAB027
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ASP1650 was given as a 2 hour intravenous (IV) infusion.

Arm title	ASP1650 Stage 2 – 600 mg/m ²
------------------	---

Arm description:

Participants received 600 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Arm type	Experimental
Investigational medicinal product name	ASP1650
Investigational medicinal product code	
Other name	IMAB027
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ASP1650 was given as a 2 hour intravenous (IV) infusion.

Arm title	ASP1650 Stage 2 – 1000 mg/m ²
------------------	--

Arm description:

Participants received 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	ASP1650
Investigational medicinal product code	
Other name	IMAB027
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ASP1650 was given as a 2 hour intravenous (IV) infusion.

Number of subjects in period 1	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²
Started	3	10	10
Treated	3	10	10
Escalated to 1000 mg/m ²	0	5	3
Completed	0	0	0
Not completed	3	10	10
Progressive Disease (PD) per RECIST	-	7	5
Death	-	-	1
Miscellaneous	-	-	-
Symptomatic Deterioration	-	2	4
Withdrawal of Consent Without Follow-Up	-	-	-

Missing	2	1	-
Withdrawal of Consent With Follow-Up	1	-	-

Number of subjects in period 1	ASP1650 Stage 2 - 600 mg/m ²	ASP1650 Stage 2 - 1000 mg/m ²
Started	10	9
Treated	10	9
Escalated to 1000 mg/m ²	2	0
Completed	0	0
Not completed	10	9
Progressive Disease (PD) per RECIST	6	3
Death	-	2
Miscellaneous	1	-
Symptomatic Deterioration	1	1
Withdrawal of Consent Without Follow-Up	1	-
Missing	1	3
Withdrawal of Consent With Follow-Up	-	-

Baseline characteristics

Reporting groups

Reporting group title	ASP1650 Stage 1/2 1-1000 mg/m ²
Reporting group description: Stage 1 participants received weekly intrasubject dose escalation of 1 mg/m ² , 10 mg/m ² , 30 mg/m ² and 100 mg/m ² ASP1650. Stage 2 participants received 100 mg/m ² , 300 mg/m ² , 600 mg/m ² or 1000 mg/m ² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants in lower doses may have escalated to 1000 mg/m ² at the discretion of the investigator and if deemed to be beneficial for the participant.	
Reporting group title	ASP1650 Stage 2 – 100 mg/m ²
Reporting group description: Participants received 100 mg/m ² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m ² at the discretion of the investigator and if deemed to be beneficial for the participant.	
Reporting group title	ASP1650 Stage 2 – 300 mg/m ²
Reporting group description: Participants received 300 mg/m ² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m ² at the discretion of the investigator and if deemed to be beneficial for the participant.	
Reporting group title	ASP1650 Stage 2 – 600 mg/m ²
Reporting group description: Participants received 600 mg/m ² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m ² at the discretion of the investigator and if deemed to be beneficial for the participant.	
Reporting group title	ASP1650 Stage 2 – 1000 mg/m ²
Reporting group description: Participants received 1000 mg/m ² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent.	

Reporting group values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²
Number of subjects	3	10	10
Age categorical Units: Subjects			

Age continuous			
The analysis population for baseline characteristics consisted of the safety analysis set (SAF), the safety population was comprised of all participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	61.3	67.9	63.9
standard deviation	± 5.69	± 8.33	± 6.82
Gender categorical Units:			
Male	0	0	0
Female	3	10	10
Race Units: Subjects			
Black or African American	0	1	1
White	3	9	9

Reporting group values	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²	Total
------------------------	--	---	-------

Number of subjects	10	9	42
Age categorical			
Units: Subjects			
Age continuous			
The analysis population for baseline characteristics consisted of the safety analysis set (SAF), the safety population was comprised of all participants who received at least 1 dose of study drug.			
Units: years			
arithmetic mean	65.8	66.9	
standard deviation	± 8.35	± 8.85	-
Gender categorical			
Units:			
Male	0	0	0
Female	10	9	42
Race			
Units: Subjects			
Black or African American	0	0	2
White	10	9	40

End points

End points reporting groups

Reporting group title	ASP1650 Stage 1/2 1-1000 mg/m ²
-----------------------	--

Reporting group description:

Stage 1 participants received weekly intrasubject dose escalation of 1 mg/m², 10 mg/m², 30 mg/m² and 100 mg/m² ASP1650. Stage 2 participants received 100 mg/m², 300 mg/m², 600 mg/m² or 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants in lower doses may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 100 mg/m ²
-----------------------	---

Reporting group description:

Participants received 100 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 300 mg/m ²
-----------------------	---

Reporting group description:

Participants received 300 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 600 mg/m ²
-----------------------	---

Reporting group description:

Participants received 600 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 1000 mg/m ²
-----------------------	--

Reporting group description:

Participants received 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent.

Subject analysis set title	Stage 2 Participants Escalated to 1000 mg/m ²
----------------------------	--

Subject analysis set type	Safety analysis
---------------------------	-----------------

Subject analysis set description:

At the completion of stage 2, participants who were administered <1000 mg/m² ASP1650 received 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent.

Subject analysis set title	Stage 1 ASP1650 1 mg/m ²
----------------------------	-------------------------------------

Subject analysis set type	Safety analysis
---------------------------	-----------------

Subject analysis set description:

Participants received a single dose of ASP1650 1 mg/m² on Day 1.

Subject analysis set title	Stage 1 ASP1650 10 mg/m ²
----------------------------	--------------------------------------

Subject analysis set type	Safety analysis
---------------------------	-----------------

Subject analysis set description:

Participants received a single dose of ASP1650 10 mg/m² on Day 8.

Subject analysis set title	Stage 1 ASP1650 30 mg/m ²
----------------------------	--------------------------------------

Subject analysis set type	Safety analysis
---------------------------	-----------------

Subject analysis set description:

Participants received a single dose of ASP1650 30 mg/m² on Day 15.

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs) ^[1]
-----------------	---

End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that: •Resulted in death •Was life-threatening •Required hospitalization or prolongation of an existing hospitalization •Resulted in disability/incapacity or •Was a congenital anomaly/birth defect in the offspring of a study participant. A treatment-emergent adverse event (TEAE) was defined as any adverse event that occurred after the

first administration of ASP1650 up to 28 days after the last dose of study drug (i.e., safety follow-up 1) or end of study, or any event that was present at baseline but worsened in severity after baseline. Severity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) v.4.03. TEAEs of special interest were identified using specific search criteria defined by Ganymed for "inner ear disorders", "pancreatitis" and "hypersensitivity/infusion reactions" events. The analysis population consisted of the SAF.

End point type	Primary
----------------	---------

End point timeframe:

From the first dose of study drug administration until 28 days after last dose of study drug or End of Study (EoS); Up to 13.31 months.

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: Statistical analysis is not applicable for this endpoint.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	10	10
Units: participants				
TEAEs	3	10	9	10
Dose-limiting toxicity	0	1	0	0
Drug-related TEAE	3	6	7	4
Procedure-related TEAE	0	1	1	0
Serious TEAE	1	5	3	2
Drug-related serious TEAE	1	1	0	0
TEAE leading to permanent discontinuation of drug	1	1	2	2
TEAE leading to study drug interruption	1	1	0	1
Grade 3 or higher TEAE	3	9	5	2
Grade 3 or higher drug-related TEAE	0	1	1	0
TEAE resulting in death	0	2	1	0
TEAE of special interest	2	1	2	2

End point values	ASP1650 Stage 2 – 1000 mg/m ²	Stage 2 Participants Escalated to 1000 mg/m ²		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	10		
Units: participants				
TEAEs	9	10		
Dose-limiting toxicity	0	0		
Drug-related TEAE	8	5		
Procedure-related TEAE	1	0		
Serious TEAE	3	3		
Drug-related serious TEAE	0	1		
TEAE leading to permanent discontinuation of drug	1	0		
TEAE leading to study drug interruption	3	2		
Grade 3 or higher TEAE	5	4		
Grade 3 or higher drug-related TEAE	1	2		

TEAE resulting in death	0	0		
TEAE of special interest	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1: Maximum Concentration (Cmax) of ASP1650

End point title	Stage 1: Maximum Concentration (Cmax) of ASP1650
End point description: The analysis population consisted of the pharmacokinetic analysis set (PKAS), which was a subset of participants from the safety analysis set for whom serum concentration data were available to facilitate derivation of at least 1 pharmacokinetic (PK) parameter and for whom the time of dosing on the day of sampling was known.	
End point type	Secondary
End point timeframe: Up to Day 2 after each infusion	

End point values	Stage 1 ASP1650 1 mg/m ²	Stage 1 ASP1650 10 mg/m ²	Stage 1 ASP1650 30 mg/m ²	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: µg/mL				
arithmetic mean (standard deviation)	0.625 (± 0.276)	6.41 (± 0.813)	22.5 (± 0.872)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Cmax of ASP1650 in Cycle 1

End point title	Stage 2: Cmax of ASP1650 in Cycle 1 ^[2]
End point description: The analysis population consisted of the PKAS.	
End point type	Secondary
End point timeframe: Up to Day 21 after infusion	

Notes:

[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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: µg/mL				
arithmetic mean (standard deviation)	101 (± 98.4)	214 (± 99.6)	326 (± 66.1)	622 (± 126)

Statistical analyses

Statistical analysis title	Statistical Assessment of Dose Proportionality
Statistical analysis description: Assessments were based on the power model (linear regression of natural log-transformed parameter and dose.	
Comparison groups	ASP1650 Stage 2 – 100 mg/m ² v ASP1650 Stage 2 – 300 mg/m ² v ASP1650 Stage 2 – 600 mg/m ² v ASP1650 Stage 2 – 1000 mg/m ²
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
Method	Regression, Linear
Parameter estimate	Slope Estimate
Point estimate	0.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.91
upper limit	1.05
Variability estimate	Standard error of the mean
Dispersion value	0.042

Secondary: Stage 2: Area Under the Concentration-Time Curve from Time Zero to Infinity (AUCinf) of ASP1650 in Cycle 1

End point title	Stage 2: Area Under the Concentration-Time Curve from Time Zero to Infinity (AUCinf) of ASP1650 in Cycle 1 ^[3]
End point description: The analysis population consisted of the PKAS.	
End point type	Secondary
End point timeframe: Up to Day 21 after infusion	

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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: h*mg/mL				
arithmetic mean (standard deviation)	6.410 (± 2.210)	19.000 (± 9.940)	45.100 (± 14.700)	89.300 (± 24.000)

Statistical analyses

Statistical analysis title	Statistical Assessment of Dose Proportionality
Statistical analysis description:	
Assessments were based on the power model (linear regression of natural log-transformed parameter and dose.	
Comparison groups	ASP1650 Stage 2 – 100 mg/m ² v ASP1650 Stage 2 – 300 mg/m ² v ASP1650 Stage 2 – 600 mg/m ² v ASP1650 Stage 2 – 1000 mg/m ²
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	1.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.99
upper limit	1.25
Variability estimate	Standard error of the mean
Dispersion value	0.077

Secondary: Stage 1: Area Under the Concentration-Time Curve from Time Zero to the Last Measureable Concentration (AUClast) of ASP1650

End point title	Stage 1: Area Under the Concentration-Time Curve from Time Zero to the Last Measureable Concentration (AUClast) of ASP1650
End point description:	
The analysis population consisted of the PKAS.	
End point type	Secondary
End point timeframe:	
Up to Day 2 after each infusion	

End point values	Stage 1 ASP1650 1 mg/m ²	Stage 1 ASP1650 10 mg/m ²	Stage 1 ASP1650 30 mg/m ²	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: h*µg/mL				
arithmetic mean (standard deviation)	9.87 (± 2.22)	124 (± 13.3)	433 (± 35.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: AUClast of ASP1650 in Cycle 1

End point title	Stage 2: AUClast of ASP1650 in Cycle 1 ^[4]
End point description: The analysis population consisted of the PKAS with available data.	
End point type	Secondary
End point timeframe: Up to Day 21 after infusion	

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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	7
Units: h*mg/mL				
arithmetic mean (standard deviation)	6.530 (± 1.700)	19.100 (± 8.150)	39.900 (± 10.200)	79.500 (± 17.700)

Statistical analyses

Statistical analysis title	Statistical Assessment of Dose Proportionality
Statistical analysis description: Assessments were based on the power model (linear regression of natural log-transformed parameter and dose.	
Comparison groups	ASP1650 Stage 2 – 100 mg/m ² v ASP1650 Stage 2 – 300 mg/m ² v ASP1650 Stage 2 – 600 mg/m ² v ASP1650 Stage 2 – 1000 mg/m ²
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	1.28

Confidence interval	
level	90 %
sides	2-sided
lower limit	1.22
upper limit	1.34
Variability estimate	Standard error of the mean
Dispersion value	0.035

Secondary: Stage 2: Percentage of AUC Due to Extrapolation from the Time of the Last Measurable Concentration to Infinity (AUCinf[%extrap]) of ASP1650 in Cycle 1

End point title	Stage 2: Percentage of AUC Due to Extrapolation from the Time of the Last Measurable Concentration to Infinity (AUCinf[%extrap]) of ASP1650 in Cycle 1 ^[5]
End point description: The analysis population consisted of the PKAS.	
End point type	Secondary
End point timeframe: Up to Day 21 after infusion	

Notes:

[5] - 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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: percentage extrapolated				
arithmetic mean (standard deviation)	9.18 (± 8.84)	9.88 (± 5.01)	14.4 (± 12.4)	14.2 (± 7.84)

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Terminal Elimination Half-Life of ASP1650 (T1/2) in Cycle 1

End point title	Stage 2: Terminal Elimination Half-Life of ASP1650 (T1/2) in Cycle 1 ^[6]
End point description: The analysis population consisted of the PKAS.	
End point type	Secondary
End point timeframe: Up to Day 21 after infusion	

Notes:

[6] - 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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: hours				
median (full range (min-max))	95.0 (76.6 to 187)	137 (53.3 to 228)	139 (95.5 to 261)	153 (91.6 to 237)

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1: Last Measurable Concentration (Clast) of ASP1650

End point title	Stage 1: Last Measurable Concentration (Clast) of ASP1650
End point description:	The analysis population consisted of the PKAS.
End point type	Secondary
End point timeframe:	Up to Day 2 after each infusion

End point values	Stage 1 ASP1650 1 mg/m ²	Stage 1 ASP1650 10 mg/m ²	Stage 1 ASP1650 30 mg/m ²	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: µg/mL				
arithmetic mean (standard deviation)	0.504 (± 0.368)	4.54 (± 0.518)	14.7 (± 2.52)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Clast of ASP1650 in Cycle 1

End point title	Stage 2: Clast of ASP1650 in Cycle 1 ^[7]
End point description:	The analysis population consisted of the PKAS with available data.
End point type	Secondary
End point timeframe:	Up to Day 21 after infusion

Notes:

[7] - 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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	7
Units: µg/mL				
arithmetic mean (standard deviation)	2.06 (± 1.74)	9.09 (± 6.58)	21.0 (± 14.2)	44.0 (± 21.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1: Time to Maximum Concentration (Tmax) of ASP1650

End point title Stage 1: Time to Maximum Concentration (Tmax) of ASP1650

End point description:

The analysis population consisted of the PKAS.

End point type Secondary

End point timeframe:

Up to Day 2 after each infusion

End point values	Stage 1 ASP1650 1 mg/m ²	Stage 1 ASP1650 10 mg/m ²	Stage 1 ASP1650 30 mg/m ²	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: hours				
median (full range (min-max))	1.68 (1.40 to 24.0)	1.50 (1.03 to 3.97)	7.95 (3.50 to 8.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Tmax of ASP1650 in Cycle 1

End point title Stage 2: Tmax of ASP1650 in Cycle 1^[8]

End point description:

The analysis population consisted of the PKAS.

End point type Secondary

End point timeframe:

Up to Day 21 after infusion

Notes:

[8] - 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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: hours				
median (full range (min-max))	2.63 (2.08 to 7.53)	2.25 (1.05 to 8.08)	2.50 (2.00 to 7.93)	3.11 (2.00 to 8.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Systemic Clearance (CL) of ASP1650 in Cycle 1

End point title	Stage 2: Systemic Clearance (CL) of ASP1650 in Cycle 1 ^[9]
-----------------	---

End point description:

The analysis population consisted of the PKAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to Day 21 after infusion

Notes:

[9] - 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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: L/h				
arithmetic mean (standard deviation)	0.0297 (± 0.0159)	0.0362 (± 0.0175)	0.0260 (± 0.00734)	0.0207 (± 0.00439)

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Volume of Distribution (Vz) of ASP1650 in Cycle 1

End point title	Stage 2: Volume of Distribution (Vz) of ASP1650 in Cycle 1 ^[10]
-----------------	--

End point description:

The analysis population consisted of the PKAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Up to Day 21 after infusion

Notes:

[10] - 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: Endpoint is only applicable for stage 2 arms/reporting groups.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: Liters				
arithmetic mean (standard deviation)	4.50 (± 1.66)	6.12 (± 2.31)	5.51 (± 0.867)	4.78 (± 1.14)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-ASP1650 Antibodies

End point title	Number of Participants with Anti-ASP1650 Antibodies
End point description: The analysis population consisted of all antidrug antibody (ADA) positive participants.	
End point type	Secondary
End point timeframe: Maximum duration of treatment; Up to 12.65 months.	

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	10	10
Units: participants	1	2	2	1

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) according to Gynecologic Cancer Intergroup

(GCIG) Criteria

End point title	Disease Control Rate (DCR) according to Gynecologic Cancer Intergroup (GCIG) Criteria
-----------------	---

End point description:

DCR was defined as the fraction (percentage) of participants with complete response (CR), partial response (PR) or stable disease (SD) as best overall response according to GCIG criteria. CR was defined as disappearance of all target lesions, any pathological lymph node must have had reduction in short axis to <10 mm, disappearance of all non-target lesions & normalization of tumor marker level with no occurrence of simultaneous appearance of new lesions. PR was defined as at least 30% decrease in the sum of the longest diameter of target lesions, referencing the screening sum longest diameter, no occurrence of simultaneous increase in size of any lesion or appearance of new lesions. SD is defined in the next endpoint. The analysis population consisted of the full analysis set (FAS), which included all participants who received at least 1 dose of study drug & met the eligibility criteria.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: percentage of participants				
number (confidence interval 95%)	50.0 (1.3 to 98.7)	10.0 (0.3 to 44.5)	40.0 (12.2 to 73.8)	30.0 (6.7 to 65.2)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of participants				
number (confidence interval 95%)	77.8 (40.0 to 97.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: DCR according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)

End point title	DCR according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)
-----------------	---

End point description:

DCR was defined as the fraction (percentage) of participants with CR or PR or SD as best overall response according to RECIST criteria. SD was defined as neither sufficient shrinkage to qualify for PR or CR nor sufficient increase to qualify for progressive disease (PD), referencing the smallest sum longest diameter recorded since treatment started, measurements must have met the SD criteria at least once after trial entry at a minimum interval not less than 6 weeks, no occurrence of simultaneous increase in size of any lesion or appearance of new lesions, evaluable lesions must have remained stable or

regressed for this category. CR and PR were defined in the previous endpoint. The analysis population consisted of the FAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	10.0 (0.3 to 44.5)	40.0 (12.2 to 73.8)	30.0 (6.7 to 65.2)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of participants				
number (confidence interval 95%)	77.8 (40.0 to 97.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: DCR according to Cancer Antigen (CA)-125 Criteria

End point title	DCR according to Cancer Antigen (CA)-125 Criteria
-----------------	---

End point description:

Disease control rate was defined as the fraction (percentage) of participants with complete response or partial response or stable disease as best overall response according to CA-125 criteria. The analysis population consisted of the FAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: percentage of participants				
number (confidence interval 95%)	100.0 (15.8 to 100.0)	40.0 (12.2 to 73.8)	80.0 (44.4 to 97.5)	90.0 (55.5 to 99.7)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of participants				
number (confidence interval 95%)	88.9 (51.8 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) according to GCIG Criteria

End point title	Objective Response Rate (ORR) according to GCIG Criteria
End point description:	
Objective response rate comprised of the fraction (percentage) of participants with CR or PR as best overall response according to GCIG criteria. The analysis population consisted of the FAS.	
End point type	Secondary
End point timeframe:	
Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.	

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	10.0 (0.3 to 44.5)	0.0 (0.0 to 0.0)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			

Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Best Overall Response According to RECIST v1.1

End point title	Percentage of Participants with Best Overall Response According to RECIST v1.1
End point description: The Best Overall Response was determined as per RECIST version 1.1 criteria alone. The analysis population consisted of the FAS.	
End point type	Secondary
End point timeframe: Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.	

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: percentage of participants				
number (not applicable)				
CR	0.0	0.0	0.0	0.0
PR	0.0	0.0	10.0	0.0
SD	0.0	10.0	30.0	30.0
PD	50.0	70.0	40.0	40.0
Not Evaluable (NE)	50.0	0.0	10.0	0.0
Not Calculated (NC)	0.0	20.0	10.0	30.0

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of participants				
number (not applicable)				
CR	0.0			
PR	0.0			
SD	77.8			
PD	22.2			
Not Evaluable (NE)	0.0			
Not Calculated (NC)	0.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Best Overall Response According to CA-125

End point title	Percentage of Participants with Best Overall Response According to CA-125
-----------------	---

End point description:

The Best Overall Response was determined as per CA-125 criteria alone. The analysis population consisted of the FAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: percentage of participants				
number (not applicable)				
Response	0.0	0.0	10.0	0.0
Non-Response	100.0	40.0	70.0	90.0
Non-Response: Non-PR/Non-PD	100.0	40.0	70.0	90.0
Non-Response: Progression	0.0	0.0	0.0	0.0
Not Available (NA)	0.0	60.0	20.0	10.0

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of participants				
number (not applicable)				
Response	0.0			
Non-Response	88.9			
Non-Response: Non-PR/Non-PD	88.9			
Non-Response: Progression	0.0			
Not Available (NA)	11.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) According to GCIG criteria

End point title	Progression Free Survival (PFS) According to GCIG criteria
-----------------	--

End point description:

PFS was calculated as the time in months from the date of first study drug dose administration to the earlier date between the first documented progression and the date of death by any cause. PFS was determined according to GCIG criteria. Participants who had not progressed either clinically or on the last scan, were censored as of the last tumor evaluation. PFS was analyzed using the Kaplan-Meier estimators. The analysis population consisted of the FAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time to PFS; Up to 30.62 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: months				
median (confidence interval 95%)	2.8 (2.7 to 3.0)	1.3 (0.5 to 1.5)	1.4 (1.2 to 5.3)	2.2 (1.2 to 3.1)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: months				
median (confidence interval 95%)	4.2 (0.6 to 4.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS According to RECIST v1.1

End point title	PFS According to RECIST v1.1
-----------------	------------------------------

End point description:

PFS was calculated as the time in months from the date of first study drug dose administration to the earlier date between the first documented progression and the date of death by any cause. PFS was determined according to RECIST version 1.1 criteria alone. Participants who had not progressed either clinically or on the last scan, were censored as of the last tumor evaluation. PFS was analyzed using the Kaplan-Meier estimators. The analysis population consisted of the FAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time to PFS; Up to 9.26 months

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	10	10	10
Units: months				
median (confidence interval 95%)	2.8 (2.7 to 3.0)	1.3 (0.5 to 1.5)	1.4 (1.2 to 5.3)	2.2 (1.2 to 3.1)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: months				
median (confidence interval 95%)	4.2 (0.6 to 6.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS According to CA-125

End point title	PFS According to CA-125
-----------------	-------------------------

End point description:

PFS was calculated as the time in months from the date of first study drug dose administration to the earlier date between the first documented progression and the date of death by any cause. PFS was determined according to CA-125 criteria alone. Participants who had not progressed either clinically or on the last scan, were censored as of the last tumor evaluation. PFS was analyzed using the Kaplan-Meier estimators. The analysis population consisted of the FAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time to PFS; Up to 30.62 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	8	7	10
Units: months				
median (confidence interval 95%)	11.7 (3.0 to 20.5)	4.1 (0.7 to 10.8)	10.2 (1.2 to 16.2)	5.9 (3.4 to 10.0)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: months				
median (confidence interval 95%)	6.1 (1.1 to 11.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio of Previous Relapse-Free Interval Vs. Current PFS

End point title	Ratio of Previous Relapse-Free Interval Vs. Current PFS ^[11]
-----------------	---

End point description:

Ratio of Previous Relapse-Free Interval vs. Current PFS was defined as the ratio between Previous Relapse-Free Interval (defined as the last time period without relapse prior to study entry) and the current PFS (time in months from the date of first study drug dose to the earlier between the date of first documented progression and the date of death by any cause; calculated based on CGIC criteria). The analysis population consisted of the FAS.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time to PFS; Up to 30.62 months.

Notes:

[11] - 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: This endpoint is not applicable to the ASP1650 Stage 1/2 1-1000 mg/m² arm/reporting group.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	10	9
Units: ratio				
arithmetic mean (standard deviation)	6.79 (± 13.396)	18.92 (± 28.122)	12.01 (± 31.343)	6.02 (± 15.380)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)
-----------------	------------------------

End point description:

TTR was defined as the duration of time from start of treatment to CR or PR per GCIG criteria. The analysis population consisted of the FAS. Only one participant in the ASP1650 Stage 2 - 300 mg/m² arm/reporting group had an overall response of CR or PR. TTR was analyzed using the Kaplan-Meier estimators. Data that was not evaluable/could not be calculated is denoted as "99999."

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[12]	0 ^[13]	1	0 ^[14]
Units: months				
median (confidence interval 95%)	(to)	(to)	99999 (2.3 to 99999)	(to)

Notes:

[12] - No participants with overall response in this arm.

[13] - No participants with overall response in this arm.

[14] - No participants with overall response in this arm.

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[15]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[15] - No participants with overall response in this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Response (DOR) per RECIST v1.1

End point title	Duration of Overall Response (DOR) per RECIST v1.1
-----------------	--

End point description:

Duration of overall response was calculated only for patients with Best Overall Response = CR or PR as per RECIST 1.1 alone. DOR was calculated as the time in months from the date of the first documented response (i.e., overall response = CR or PR) to the earlier between the date of the first documentation of disease progression and the date of death. The analysis population consisted of the FAS. Only one participant in the ASP1650 Stage 2 - 300 mg/m² arm/reporting group had overall response, the only evaluable data was the median 95% CI, which was 4.6 months. DOR was analyzed using the Kaplan-Meier estimators. Due to a validation rule, ASP1650 Stage 2 - 300 mg/m² arm/reporting group's median of 4.6 months cannot be included in the data table and is indicated as "99999." Data that was

not evaluable/could not be calculated is also denoted as "99999."

End point type	Secondary
End point timeframe:	
Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.	

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[16]	0 ^[17]	1	0 ^[18]
Units: months				
median (confidence interval 95%)	(to)	(to)	99999 (99999 to 99999)	(to)

Notes:

[16] - No participants with overall response in this arm.

[17] - No participants with overall response in this arm.

[18] - No participants with overall response in this arm.

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[19]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[19] - No participants with overall response in this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Stable Disease (DSD) per RECIST v1.1

End point title	Duration of Stable Disease (DSD) per RECIST v1.1
End point description:	
For participants with documented progression or death, the duration of SD was calculated as the time in months from the date of first documented SD response (i.e., overall response = CR or PR or SD) to the earlier between the date of the first documentation of disease progression and the date of death. For participants without documented progression or death (i.e., censored participants for the analysis), the duration of SD was calculated as the time in months from the date of first documented SD response (i.e., overall response = CR or PR or SD) to the date of the last overall response evaluation prior to dose level escalation to 1000 mg/m ² , if that occurred. Due to the validation rule, the ASP1650 Stage 2 – 100 mg/m ² arm/reporting group median of 7.9 months cannot be included in the data table and is denoted as "99999." DSD was analyzed using the Kaplan-Meier estimators. Data that was not evaluable/could not be calculated is also denoted as "99999."	
End point type	Secondary
End point timeframe:	
Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.	

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[20]	1	4	3
Units: months				
median (confidence interval 95%)	(to)	99999 (99999 to 99999)	3.5 (1.1 to 4.7)	1.6 (1.4 to 2.8)

Notes:

[20] - No participants with stable disease in this arm.

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: months				
median (confidence interval 95%)	2.8 (0.9 to 5.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time from the date of the first study drug administration until the date of death by any cause. Any participant not known to have died at the time of analysis was censored based on the last recorded date on which the participant was known to be alive. OS was analyzed using the Kaplan-Meier estimators. The analysis population consisted of the FAS. Data that was not evaluable/could not be calculated is denoted as "99999."	
End point type	Secondary
End point timeframe:	
Maximum duration of time to OS; Up to 33.87 months.	

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	8	7	9
Units: months				
median (confidence interval 95%)	11.7 (3.0 to 20.5)	4.1 (0.7 to 10.8)	10.2 (1.2 to 99999)	7.4 (3.4 to 12.3)

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
------------------	--	--	--	--

Subject group type	Reporting group			
Number of subjects analysed	8			
Units: months				
median (confidence interval 95%)	6.9 (1.1 to 15.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Terminal Elimination Half-Life (T1/2) of CA-125

End point title	Apparent Terminal Elimination Half-Life (T1/2) of CA-125
-----------------	--

End point description:

T_{1/2} of CA-125 was defined as the time from first study drug dose to the date half or less of the baseline CA-125 value had been reached for the first time. The analysis population consisted of the per-protocol analysis set (PPS), which included all FAS participants, excluding those for whom a major protocol deviation had been identified.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time to PFS; Up to 30.62 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[21]	0 ^[22]	0 ^[23]	0 ^[24]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[21] - No participants reached half or less of baseline CA-125 in this arm.

[22] - No participants reached half or less of baseline CA-125 in this arm.

[23] - No participants reached half or less of baseline CA-125 in this arm.

[24] - No participants reached half or less of baseline CA-125 in this arm.

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[25]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[25] - No participants reached half or less of baseline CA-125 in this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Nadir of CA-125

End point title	Time to Nadir of CA-125
-----------------	-------------------------

End point description:

The nadir of CA-125 was defined as the lowest value of CA-125 during the treatment period. The time to nadir of CA-125 (months) was calculated as follows: Time to nadir of CA-125 (months) = (date of nadir value of CA-125 sampling – date of first study drug dose +1)/30.4375. If the nadir occurred on several different occasions, the first in time was taken. Due to a validation rule, ASP1650 Stage 2 - 1000 mg/m² arm/reporting group median of 1.7 months could not be included in the data table and is denoted as "99999." Time to nadir of CA-125 was analyzed using the Kaplan-Meier estimators. The analysis population consisted of the PPS. Data that was not evaluable/could not be calculated is also denoted as "99999."

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time to PFS; Up to 30.62 months.

End point values	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[26]	2	3	2
Units: months				
median (confidence interval 95%)	(to)	1.3 (1.1 to 1.4)	1.4 (1.4 to 1.5)	2.3 (1.4 to 3.2)

Notes:

[26] - No participants reached time to nadir of CA-125 in this arm.

End point values	ASP1650 Stage 2 – 1000 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression Ratio

End point title	Time to Progression Ratio ^[27]
-----------------	---

End point description:

Time to Progression Ratio was defined as the ratio of time to progression (months) prior to dose escalation and time to progression (months) after dose escalation. The analysis population consisted of the FAS. Only Stage 2 Participants Escalated to 1000 mg/m² is included, however the data is shown by dose as assigned at Stage 2 entry.

End point type	Secondary
----------------	-----------

End point timeframe:

Maximum duration of time from first dose of study drug administration to EoS; Up to 13.31 months.

Notes:

[27] - 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: This endpoint is not applicable to the ASP1650 Stage 1/2 1-1000 mg/m² arm/reporting group.

End point values	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	2	0 ^[28]
Units: ratio				
arithmetic mean (standard deviation)	1.6 (± 1.05)	0.9 (± 0.61)	16.3 (± 21.68)	()

Notes:

[28] - No participants had time to progression ratio data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug administration until 28 days after last dose of study drug or End of Study (EoS); Up to 13.31 months.

Adverse event reporting additional description:

The total number of deaths (all causes) includes deaths reported after the time frame above.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	16.1
--------------------	------

Reporting groups

Reporting group title	ASP1650 Stage 1/2 1-1000 mg/m ²
-----------------------	--

Reporting group description:

Stage 1 participants received weekly intrasubject dose escalation of 1 mg/m², 10 mg/m², 30 mg/m² and 100 mg/m² ASP1650. Stage 2 participants received 100 mg/m², 300 mg/m², 600 mg/m² or 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants in lower doses may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 100 mg/m ²
-----------------------	---

Reporting group description:

Participants received 300 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 300 mg/m ²
-----------------------	---

Reporting group description:

Participants received 300 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 600 mg/m ²
-----------------------	---

Reporting group description:

Participants received 600 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent. Participants may have escalated to 1000 mg/m² at the discretion of the investigator and if deemed to be beneficial for the participant.

Reporting group title	ASP1650 Stage 2 – 1000 mg/m ²
-----------------------	--

Reporting group description:

Participants received 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent.

Reporting group title	Stage 2 Participants Escalated to 1000 mg/m ²
-----------------------	--

Reporting group description:

At the completion of stage 2, participants who were administered <1000 mg/m² ASP1650 received 1000 mg/m² ASP1650 every 3 weeks until progressive disease, toxicity or withdrawal of consent.

Serious adverse events	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	5 / 10 (50.00%)	3 / 10 (30.00%)
number of deaths (all causes)	3	5	5
number of deaths resulting from adverse events	0	1	1

Investigations			
Medical observation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Ovarian cancer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Euthanasia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General physical health deterioration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (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
Obstruction gastric			

subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Portal vein occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (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
Pleuritic pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (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
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (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

Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (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

Serious adverse events	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²	Stage 2 Participants Escalated to 1000 mg/m ²
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	3 / 9 (33.33%)	3 / 10 (30.00%)
number of deaths (all causes)	8	8	6
number of deaths resulting from adverse events	0	0	0
Investigations			
Medical observation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Acute prerenal failure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (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
Nervous system disorders			
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device related infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Euthanasia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (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
Medical device complication			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (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
Ileus			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (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
Hepatobiliary disorders			
Portal vein occlusion			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
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			
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
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			
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	ASP1650 Stage 1/2 1-1000 mg/m ²	ASP1650 Stage 2 – 100 mg/m ²	ASP1650 Stage 2 – 300 mg/m ²
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	10 / 10 (100.00%)	8 / 10 (80.00%)
Vascular disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypertensive crisis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Varicose vein			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Abdominal cavity drainage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	2
Cataract operation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Central venous catheterisation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Axillary pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	4 / 10 (40.00%)	3 / 10 (30.00%)
occurrences (all)	0	7	5
General physical health deterioration			

subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Multi-organ failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	4 / 10 (40.00%)
occurrences (all)	0	0	4
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Bronchial wall thickening			

subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	3 / 3 (100.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	5	0	1
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypopnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal mucosal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Obstructive airways disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pleuritic pain			

subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	2
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Blood bilirubin increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Breath sounds abnormal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	3	0	3
Lymph node palpable			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Transfusion reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Atrioventricular block			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Conduction disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Disorientation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Paresis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Trigeminal neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymph node pain			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Tympanic membrane disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 10 (10.00%) 1	1 / 10 (10.00%) 1
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Dry eye subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1
Eye swelling subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	3 / 10 (30.00%) 4	3 / 10 (30.00%) 4
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Abdominal tenderness			

subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	3 / 10 (30.00%)
occurrences (all)	0	2	4
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	2 / 10 (20.00%)	4 / 10 (40.00%)
occurrences (all)	1	2	5
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eiploic appendagitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Faecal incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastric ulcer			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal obstruction			

subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Intestinal perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Melaena			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	4 / 10 (40.00%)
occurrences (all)	0	1	4
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Subileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	2 / 10 (20.00%)
occurrences (all)	1	1	3
Vomiting projectile			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Skin and subcutaneous tissue disorders			
Night sweats subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Alopecia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Lividity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Nail disorder subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Skin burning sensation subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Xeroderma subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0
Renal and urinary disorders			

Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oliguria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyelocaliectasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	3 / 10 (30.00%)	0 / 10 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	3 / 10 (30.00%)
occurrences (all)	0	1	5
Groin pain			

subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	3 / 10 (30.00%)
occurrences (all)	0	1	3
Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hyperkalaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Hypomagnesaemia			
subjects affected / exposed	3 / 3 (100.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	4	1	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Metabolic disorder			
subjects affected / exposed	2 / 3 (66.67%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Xerophthalmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	ASP1650 Stage 2 – 600 mg/m ²	ASP1650 Stage 2 – 1000 mg/m ²	Stage 2 Participants Escalated to 1000 mg/m ²
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	9 / 9 (100.00%)	9 / 10 (90.00%)
Vascular disorders			
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypertension			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypertensive crisis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Thrombophlebitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Abdominal cavity drainage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cataract operation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Central venous catheterisation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Axillary pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 10 (30.00%)	6 / 9 (66.67%)	2 / 10 (20.00%)
occurrences (all)	4	13	5
General physical health deterioration			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Generalised oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Local swelling			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Localised oedema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Multi-organ failure			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Bronchial wall thickening			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 10 (10.00%)	3 / 9 (33.33%)	1 / 10 (10.00%)
occurrences (all)	3	4	1
Dysphonia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	3 / 10 (30.00%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	4	1	2
Dyspnoea exertional			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypopnoea			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nasal mucosal disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Obstructive airways disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Pleuritic pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Depressed mood subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Sleep disorder subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Tension subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 9 (22.22%) 2	0 / 10 (0.00%) 0
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Amylase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 2	1 / 10 (10.00%) 1
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Blood creatinine increased			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Lymph node palpable			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Lymphocyte count increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Transaminases increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	1 / 10 (10.00%) 1
Weight increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Transfusion reaction subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Cardiac disorders			
Atrial flutter subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Atrioventricular block subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 3	0 / 10 (0.00%) 0
Atrioventricular block first degree subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Conduction disorder			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ventricular extrasystoles			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Paresis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Somnolence subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Trigeminal neuralgia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	0 / 9 (0.00%) 0	1 / 10 (10.00%) 2
Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Lymph node pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 2	0 / 10 (0.00%) 0
Ear and labyrinth disorders			
Tinnitus subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Tympanic membrane disorder subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Eye disorders			
Cataract subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Dry eye			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Abdominal pain upper			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	2	2	0
Abdominal tenderness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	2 / 10 (20.00%)	3 / 9 (33.33%)	1 / 10 (10.00%)
occurrences (all)	2	3	1
Diarrhoea			
subjects affected / exposed	2 / 10 (20.00%)	4 / 9 (44.44%)	1 / 10 (10.00%)
occurrences (all)	2	6	1
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Dysphagia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Epiplonic appendagitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Faecal incontinence			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastric ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Intestinal perforation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	4 / 10 (40.00%)	4 / 9 (44.44%)	2 / 10 (20.00%)
occurrences (all)	5	5	2
Small intestinal obstruction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Stomatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Subileus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	3 / 10 (30.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	6	2	1
Vomiting projectile			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Decubitus ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Lividity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nail disorder			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	2 / 10 (20.00%)
occurrences (all)	0	2	2
Skin burning sensation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Flank pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oliguria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pyelocaliectasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Renal impairment subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	1 / 10 (10.00%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	0 / 9 (0.00%) 0	2 / 10 (20.00%) 2
Groin pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	2 / 10 (20.00%) 2
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	1 / 10 (10.00%) 3
Pain in extremity subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Infections and infestations			
Candida infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Infection			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 9 (22.22%) 2	0 / 10 (0.00%) 0
Metabolism and nutrition disorders			
Oedema			
subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Decreased appetite			
subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	1 / 9 (11.11%) 2	2 / 10 (20.00%) 2
Hypercholesterolaemia			
subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hyperkalaemia			
subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Hypokalaemia			
subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	1 / 10 (10.00%) 1
Hypomagnesaemia			
subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	2 / 9 (22.22%) 2	0 / 10 (0.00%) 0
Hyponatraemia			
subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hypophosphataemia			
subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 2	0 / 10 (0.00%) 0
Metabolic disorder			
subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Xerophthalmia			
subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

This study was conducted by Ganymed AG, a company that was acquired by Astellas in December of 2016.
--

Notes: