Clinical trial results:
A phase I/Ib open-label, multi-center dose escalation study of JBH492 in patients with relapsed/refractory chronic lymphocytic leukemia (CLL) and Non-Hodgkin's Lymphoma (NHL)

Summary

EudraCT number	2019-002666-12
Trial protocol	FI DE
Global end of trial date	05 September 2024

Results information

Result version number	v1 (current)
This version publication date	19 July 2025
First version publication date	19 July 2025

Trial information

Trial identification

Sponsor protocol code	CJBH492A12101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04240704
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Lichtstrasse 35, Basel, Switzerland, 4056
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	05 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 September 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To characterize safety, tolerability, and maximum tolerated dose (MTD)/recommended dose (RD) for expansion of JBH492 single agent in participants with relapsed/refractory (r/r) CLL and r/r NHL.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 4
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Israel: 2
Worldwide total number of subjects	25
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

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

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	10
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in 8 investigative sites in 7 countries.

Pre-assignment

Screening details:

The screening period began once patients had signed the study informed consent. Screening evaluations had to be completed within 28 days prior to the first dose of study treatment. After screening, the treatment period started on Cycle 1 Day 1.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	JBH492 0.4 mg/kg

Arm description:

JBH492 0.4 mg/kg intravenously once every 3 weeks

Arm type	Experimental
Investigational medicinal product name	JBH492
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.4 mg/Kg once every 3 weeks

Arm title	JBH492 0.8 mg/kg

Arm description:

JBH492 0.8 mg/kg intravenously once every 3 weeks

Arm type	Experimental
Investigational medicinal product name	JBH492
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.8 mg/Kg once every 3 weeks

Arm title	JBH492 1.6mg/kg

Arm description:

JBH492 1.6 mg/kg intravenously once every 3 weeks

Arm type	Experimental
Investigational medicinal product name	JBH492
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 1.6 mg/Kg once every 3 weeks	

Arm title	JBH492 2.4mg/kg
Arm description: JBH492 2.4 mg/kg intravenously once every 3 weeks	
Arm type	Experimental
Investigational medicinal product name	JBH492
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 2.4 mg/Kg once every 3 weeks	

Arm title	JHB492 3.6mg/kg
Arm description: JBH492 3.6 mg/kg intravenously once every 3 weeks	
Arm type	Experimental
Investigational medicinal product name	JBH492
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 3.6 mg/Kg once every 3 weeks	

Number of subjects in period 1	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg
Started	4	3	5
Completed	0	0	0
Not completed	4	3	5
Participant decision	-	-	-
Death	1	-	-
Adverse event	-	-	-
Progressive disease	3	3	5

Number of subjects in period 1	JBH492 2.4mg/kg	JHB492 3.6mg/kg
Started	7	6
Completed	0	0
Not completed	7	6
Participant decision	-	1
Death	1	-
Adverse event	-	2

Progressive disease	6	3

Baseline characteristics

Reporting groups	
Reporting group title	JBH492 0.4 mg/kg
Reporting group description: JBH492 0.4 mg/kg intravenously once every 3 weeks	
Reporting group title	JBH492 0.8 mg/kg
Reporting group description: JBH492 0.8 mg/kg intravenously once every 3 weeks	
Reporting group title	JBH492 1.6mg/kg
Reporting group description: JBH492 1.6 mg/kg intravenously once every 3 weeks	
Reporting group title	JBH492 2.4mg/kg
Reporting group description: JBH492 2.4 mg/kg intravenously once every 3 weeks	
Reporting group title	JHB492 3.6mg/kg
Reporting group description: JBH492 3.6 mg/kg intravenously once every 3 weeks	

Reporting group values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg
Number of subjects	4	3	5
Age Categorical Units: Participants			
18 - < 65 years	1	0	2
65 - < 85 years	2	3	3
>= 85 years	1	0	0
Age Continuous Units: years			
arithmetic mean	75	71	64.4
standard deviation	± 9.06	± 3.61	± 10.36
Sex: Female, Male Units: Participants			
Female	2	0	1
Male	2	3	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	2	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	JBH492 2.4mg/kg	JHB492 3.6mg/kg	Total
Number of subjects	7	6	25

Age Categorical Units: Participants			
18 - < 65 years	3	4	10
65 - < 85 years	4	2	14
>= 85 years	0	0	1
Age Continuous Units: years			
arithmetic mean	65.1	59.5	
standard deviation	± 10.09	± 13.81	-
Sex: Female, Male Units: Participants			
Female	3	2	8
Male	4	4	17
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	6
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	5	4	17
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	JBH492 0.4 mg/kg
Reporting group description: JBH492 0.4 mg/kg intravenously once every 3 weeks	
Reporting group title	JBH492 0.8 mg/kg
Reporting group description: JBH492 0.8 mg/kg intravenously once every 3 weeks	
Reporting group title	JBH492 1.6mg/kg
Reporting group description: JBH492 1.6 mg/kg intravenously once every 3 weeks	
Reporting group title	JBH492 2.4mg/kg
Reporting group description: JBH492 2.4 mg/kg intravenously once every 3 weeks	
Reporting group title	JHB492 3.6mg/kg
Reporting group description: JBH492 3.6 mg/kg intravenously once every 3 weeks	
Subject analysis set title	Low dose JBH492 0.4/0.8/1.6 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: JBH492 0.4, 0.8 and 1.6 mg/kg intravenously once every 3 weeks	
Subject analysis set title	High dose JBH492 2.4/3.6 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description: JBH492 2.4 and 3.6 mg/kg intravenously once every 3 weeks	

Primary: Number of participants with dose limiting toxicities (DLTs)

End point title	Number of participants with dose limiting toxicities (DLTs)[1]

End point description:

A dose-limiting toxicity (DLT) is defined as an adverse event (AE) or abnormal laboratory value that occurs during the first cycle of treatment with JBH492 and meets any of the protocol specified criteria, unless incontrovertibly related to underlying disease, intercurrent illness or concomitant medications.

AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5. For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

First cycle of treatment (21 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis testing was planned for this primary endpoint

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	5	7
Units: Participants	0	0	1	0

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with on treatment Adverse Events (AEs)

End point title	Number of participants with on treatment Adverse Events

End point description:

An adverse event (treatment emergent) is defined as the appearance of (or worsening of any pre-existing) undesirable sign(s), symptom(s), or medical condition(s) that occur after patient's signed informed consent has been obtained.

AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5. For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

From treatment day 1 until 30 days post last treatment up to approximately 1.6 years

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis testing was planned for this primary endpoint

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: Participants				
AEs	4	3	5	7
AEs suspected to be treatment related	1	1	3	6
AEs requiring additional therapy	3	2	3	5

End point values	JHB492 3.6mg/kg			

Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants				
AEs	5			
AEs suspected to be treatment related	5			
AEs requiring additional therapy	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with on treatment Serious Adverse Events (SAEs)

End point title	Number of participants with on treatment Serious Adverse Events (SAEs)[3]

End point description:

A Serious adverse event (SAE) is defined as one of the following:
• Is fatal or life-threatening
• Results in persistent or significant disability/incapacity
• Constitutes a congenital anomaly/birth defect
• Is medically significant
• Requires inpatient hospitalization or prolongation of existing hospitalization.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

From treatment day 1 until 30 days post last treatment up to approximately 1.6 years

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis testing was planned for this primary endpoint

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: Participants				
SAEs	1	1	0	2
SAEs suspected to be treatment related	0	0	0	0

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants				
SAEs	3			
SAEs suspected to be treatment related	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with dose interruptions and dose reductions

End point title	Number of participants with dose interruptions and dose reductions[4]

End point description:

Tolerability measured by the number of subjects who have interruptions or reductions of study treatment.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

From first dose of study treatment until last dose up to approximately 1.5 years

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis testing was planned for this primary endpoint

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: Participants				
At least one dose reduction or interruption	0	0	0	3
Participants with at least one dose reduction	0	0	0	1
Participants with at least one dose interruption	0	0	0	2

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants				
At least one dose reduction or interruption	2			
Participants with at least one dose reduction	2			
Participants with at least one dose interruption	0			

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative dose

End point title	Cumulative dose[5]

End point description:

Tolerability was measured by the cumulative dose of study drug. Cumulative dose is defined as the total dose given during the study treatment exposure.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

From first dose of study treatment until last dose up to approximately 1.5 years

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis testing was planned for this primary endpoint

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: mg/Kg				
median (full range (min-max))	1.00 (0.4 to 1.2)	0.80 (0.8 to 0.8)	4.80 (1.6 to 9.6)	16.80 (2.4 to 45.6)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: mg/Kg				
median (full range (min-max))	7.20 (3.6 to 57.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Relative dose intensity

End point title	Relative dose intensity[6]

End point description:

Tolerability was measured by the relative dose intensity of study drug. Relative Dose intensity for subjects with non-zero duration of exposure is computed as the ratio of dose intensity and planned dose intensity.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

From baseline until last dose os study treatment up to approximately 1.5 years

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical hypothesis testing was planned for this primary endpoint

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: Ratio				
median (full range (min-max))	1.000 (1.00 to 1.00)	1.000 (1.00 to 1.00)	1.000 (1.00 to 1.00)	1.000 (1.00 to 1.00)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Ratio				
median (full range (min-max))	1.000 (1.00 to 1.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response (BOR) in CLL participants

End point title	Best overall response (BOR) in CLL participants

End point description:

The best overall response (BOR) is the best response recorded in a patient from the start of treatment until disease progression.
Efficacy was based on local investigator assessment per international workshop on Chronic Lymphocytic Leukemia (iwCLL).

End point type	Secondary

End point timeframe:

From baseline up to 157 days after last dose

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[7]	0[8]	1	0[9]
Units: Participants				
Progressive disease			1	

Notes:

[7] - no CLL participants in this arm

[8] - no CLL participants in this arm

[9] - no CLL participants in this arm

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: Participants				

Progressive disease				

Notes:

[10] - no CLL participants in this arm

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response (BOR) in NHL participants

End point title	Best overall response (BOR) in NHL participants

End point description:

The best overall response (BOR) is the best response recorded in a patient from the start of treatment until disease progression.
Efficacy was based on local investigator assessment per Lugano criteria.

End point type	Secondary

End point timeframe:

From baseline up to 157 days after last dose

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	7
Units: Participants				
Complete Response (CR)	0	0	0	0
Partial Response (PR)	0	0	0	3
Stable Disease	0	0	1	0
Progressive Disease	3	3	3	4
Unkown	1	0	0	0

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants				
Complete Response (CR)	1			
Partial Response (PR)	1			
Stable Disease	0			
Progressive Disease	3			
Unkown	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR) in NHL participants

End point title	Overall response rate (ORR) in NHL participants

End point description:

The overall response rate (ORR), defined as the proportion of subjects with best overall response (BOR) of complete response (CR) or partial response (PR).
Efficacy was based on local investigator assessment per Lugano criteria.

End point type	Secondary

End point timeframe:

From baseline up to 157 days after last dose

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	4	7
Units: Participants	0	0	0	3

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Participants	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) in NHL participants

End point title	Duration of Response (DOR) in NHL participants

End point description:

The time between the date of first documented response (CR or PR) and the date of first documented progression or death due to underlying cancer. Duration of response was to be estimated using the Kaplan-Meier method.
Efficacy was based on local investigator assessment per Lugano criteria.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating ‘not applicable’). Therefore, not applicable values are indicated as ‘999’.

End point type	Secondary

End point timeframe:

From baseline up to 157 days after last dose

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	3[14]
Units: Months				
arithmetic mean (standard deviation)	()	()	()	999 (± 999)

Notes:

[11] - No participants with documented response in this arm

[12] - No participants with documented response in this arm

[13] - No participants with documented response in this arm

[14] - NA: Not estimable due to insufficient number of participants with events

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	2[15]			
Units: Months				
arithmetic mean (standard deviation)	999 (± 999)			

Notes:

[15] - NA: Not estimable due to insufficient number of participants with events

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameter AUClast JBH492 total antibody and JBH492 total ADC

End point title	Pharmacokinetics (PK) parameter AUClast JBH492 total antibody and JBH492 total ADC

End point description:

The area under the concentration-time curve (AUC) of JBH492 from time zero to the last measurable concentration sampling time (tlast) for total antibody and total antibody-drug-conjugate based on serum concentrations.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: hours * ug/mL				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody (cycle 1) n=4,3,5,7,6	1080 (± 57.6)	1460 (± 18.0)	4450 (± 36.4)	9330 (± 35.6)
JBH492 total antibody (cycle 3) n=2,0,3,5,2	1320 (± 0.8)	999 (± 999)	3290 (± 255.2)	17600 (± 31.8)
JBH492 total ADC (cycle 1) n=4,3,5,7,6	598 (± 38.7)	822 (± 41.1)	2280 (± 18.1)	5590 (± 29.0)

JBH492 total ADC (cycle 3) n=2,0,3,5,2	434 (± 20.4)	999 (± 999)	1440 (± 61.9)	5630 (± 21.5)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours * ug/mL				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody (cycle 1) n=4,3,5,7,6	9300 (± 99.6)			
JBH492 total antibody (cycle 3) n=2,0,3,5,2	20600 (± 38.3)			
JBH492 total ADC (cycle 1) n=4,3,5,7,6	6030 (± 53.6)			
JBH492 total ADC (cycle 3) n=2,0,3,5,2	7090 (± 28.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) in NHL participants

End point title	Progression Free Survival (PFS) in NHL participants

End point description:

PFS is defined as the time from the date of start of treatment to the date of the first documented progression or death due to any cause. Efficacy was based on local investigator assessment per Lugano criteria.
Participants were summarized into two pooled groups low dose and high dose cohorts.

End point type	Secondary

End point timeframe:

From baseline up to 157 days after last dose

End point values	Low dose JBH492 0.4/0.8/1.6	High dose JBH492 2.4/3.6 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	13		
Units: Months				
median (inter-quartile range (Q1-Q3))	1.0 (0.7 to 1.9)	2.1 (2.1 to 8.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameter AUClast DM4 and sDM4

End point title	Pharmacokinetics (PK) parameter AUClast DM4 and sDM4

End point description:

The area under the concentration-time curve (AUC) of JBH492 from time zero to the last measurable concentration sampling time (tlast) for DM4 and sDM4 based on plasma concentrations.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
DM4 (cycle 1) n=4,3,5,7,6	4.86 (± 195.2)	14.6 (± 35.8)	77.9 (± 23.1)	142 (± 23.6)
DM4 (cycle 3) n=2,0,3,5,2	11.8 (± 5.8)	999 (± 999)	47.2 (± 30.3)	231 (± 41.3)
sDM4 (cycle 1) n=4,3,5,7,6	54.1 (± 15.4)	135 (± 32.1)	547 (± 43.9)	435 (± 52.4)
sDM4 (cycle 3) n=2,0,3,5,2	154 (± 10.1)	999 (± 999)	522 (± 378.6)	784 (± 64.7)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
DM4 (cycle 1) n=4,3,5,7,6	177 (± 48.2)			
DM4 (cycle 3) n=2,0,3,5,2	248 (± 16.2)			
sDM4 (cycle 1) n=4,3,5,7,6	332 (± 348.2)			
sDM4 (cycle 3) n=2,0,3,5,2	562 (± 86.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter AUCinf JBH492 total antibody and JBH492 total ADC

End point title	PK parameter AUCinf JBH492 total antibody and JBH492 total ADC

End point description:

The AUC from time zero to infinity (mass × time × volume-1) for total antibody and total antibody-drug-conjugate based on
serum concentrations of JBH492 total antibody and JBH492 total ADC.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: hour*ug/mL				
geometric mean (geometric coefficient of variation)				
JBH942 total antibody n=1,0,2,0,1	489 (± 999)	999 (± 999)	3700 (± 66.2)	999 (± 999)
JBH942 total ADC n=4,3,5,7,5	643 (± 36.1)	900 (± 32.9)	2380 (± 17.6)	5900 (± 29.9)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hour*ug/mL				
geometric mean (geometric coefficient of variation)				
JBH942 total antibody n=1,0,2,0,1	17500 (± 999)			
JBH942 total ADC n=4,3,5,7,5	7660 (± 19.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter AUCinf DM4 and sDM4

End point title	PK parameter AUCinf DM4 and sDM4

End point description:

The AUC from time zero to infinity (mass × time × volume-1) for DM4 and sDM4 based on plasma concentrations of DM4 and sDM4.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[16]	0[17]	2	5
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
DM4 n=0,0,1,5,4	()	()	99.4 (± 999)	158 (± 19.7)
sDM4 n=0,0,2,0,2	()	()	614 (± 17.1)	999 (± 99)

Notes:

[16] - no participants with an available value for this endpoint

[17] - no participants with an available value for this endpoint

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
DM4 n=0,0,1,5,4	226 (± 25.0)			
sDM4 n=0,0,2,0,2	601 (± 70.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter AUCtau JBH492 total antibody and JBH492 total ADC

End point title	PK parameter AUCtau JBH492 total antibody and JBH492 total ADC

End point description:

The AUC calculated to the end of a dosing interval (tau) (mass × time × volume-1) for total antibody and total antibody-drug-conjugate based on serum concentrations of JBH492 total antibody and JBH492 total ADC.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 3. One cycle=21 days

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0[18]	1	5
Units: hour*ug/mL				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody n=0,0,0,0,0	999 (± 999)	()	999 (± 999)	999 (± 999)
JBH492 total ADC n=1,0,1,5,2	547 (± 999)	()	2650 (± 999)	5730 (± 21.4)

Notes:

[18] - No participants with available value for endpoint

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: hour*ug/mL				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody n=0,0,0,0,0	999 (± 999)			
JBH492 total ADC n=1,0,1,5,2	7100 (± 28)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter AUCtau DM4 and sDM4

End point title	PK parameter AUCtau DM4 and sDM4

End point description:

The AUC calculated to the end of a dosing interval (tau) (mass × time × volume-1) for four DM4 and sDM4 based on plasma concentrations of DM4 and sDM4.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 3. One cycle=21 days

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[19]	0[20]	0[21]	5
Units: hour*ng/mL				
geometric mean (geometric coefficient of variation)				
DM4	()	()	()	239 (± 40.3)
sDM4	()	()	()	1100 (± 76.9)

Notes:

[19] - no participants with an available value for this endpoint

[20] - no participants with an available value for this endpoint

[21] - no participants with an available value for this endpoint

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: hour*ng/mL				
geometric mean (geometric coefficient				

of variation)				
DM4	248 (± 16.2)			
sDM4	563 (± 86.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter Cmax JBH492 total antibody and JBH492 total ADC

End point title	PK parameter Cmax JBH492 total antibody and JBH492 total ADC

End point description:

The maximum (peak)observed serum drug concentration (mass × volume-1) for total antibody and total antibody-drug-conjugate based on serum concentrations of JBH492 total antibody and JBH492 total ADC.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody (Cycle 1)	6.26 (± 38.4)	10.5 (± 41.0)	27.6 (± 23.0)	44.7 (± 14.1)
JBH492 total antibody (Cycle 3) n=2,0,3,5,2	6.8 (± 28.2)	999 (± 999)	30.3 (± 17.6)	71.7 (± 14.3)
JBH492 total ADC (Cycle 1)	7.03 (± 30.9)	7.81 (± 74.2)	27.2 (± 11.5)	49.4 (± 17.5)
JBH492 total ADC (Cycle 3) n=2,0,3,5,2	5.11 (± 37.8)	999 (± 999)	24.8 (± 19.4)	53.8 (± 15.3)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody (Cycle 1)	56.1 (± 19.0)			
JBH492 total antibody (Cycle 3) n=2,0,3,5,2	65.2 (± 49.5)			
JBH492 total ADC (Cycle 1)	66.4 (± 22.0)			
JBH492 total ADC (Cycle 3) n=2,0,3,5,2	53.2 (± 17.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter Cmax DM4 and sDM4

End point title	PK parameter Cmax DM4 and sDM4

End point description:

The maximum (peak)observed serum drug concentration (mass × volume-1) for DM4 and sDM4 based on plasma concentrations of DM4 and sDM4.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
DM4 (Cycle 1)	0.316 (± 28.1)	0.571 (± 1.2)	1.24 (± 55.6)	2.07 (± 19.6)
DM4 (Cycle 3) n=2,0,3,5,2	0.305 (± 6.7)	999 (± 999)	2.05 (± 238.8)	4.91 (± 320.2)
sDM4 (Cycle 1)	0.196 (± 26.1)	0.567 (± 25.0)	2.01 (± 24.9)	1.64 (± 53.9)
sDM4 (Cycle 3) n=2,0,3,5,2	0.522 (± 9.4)	999 (± 999)	4.62 (± 70.0)	3.32 (± 65.9)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
DM4 (Cycle 1)	2.48 (± 42.7)			
DM4 (Cycle 3) n=2,0,3,5,2	2.43 (± 37.2)			
sDM4 (Cycle 1)	2.19 (± 55.6)			
sDM4 (Cycle 3) n=2,0,3,5,2	2.46 (± 84.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter Tmax JBH492 total antibody and JBH492 total ADC

End point title	PK parameter Tmax JBH492 total antibody and JBH492 total ADC

End point description:

The time to reach maximum (peak) drug concentration (time) for total antibody and total antibody-drug-conjugate based on serum concentrations of JBH492 total antibody and JBH492 total ADC.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: hours				
median (full range (min-max))				
JBH492 total antibody (Cycle 1)	13.2 (1.07 to 25.1)	3.9 (1.92 to 71)	1.07 (1 to 5.12)	2.05 (1 to 2.12)
JBH492 total antibody (Cycle 3) n=2,0,3,5,2	86 (4.88 to 167)	999 (999 to 999)	3.92 (1.17 to 4)	2 (1.05 to 2.48)
JBH492 total ADC (Cycle 1)	2.12 (1.07 to 24.3)	2.03 (1.92 to 3.9)	4.08 (1.02 to 5.12)	2.08 (1 to 5.17)
JBH492 total ADC (Cycle 3) n=2,0,3,5,2	25.4 (2.08 to 48.6)	999 (999 to 999)	3.92 (1.17 to 4)	2.48 (1.08 to 5.08)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
median (full range (min-max))				
JBH492 total antibody (Cycle 1)	2.95 (1 to 5)			
JBH492 total antibody (Cycle 3) n=2,0,3,5,2	11.6 (1 to 22.2)			
JBH492 total ADC (Cycle 1)	4.05 (1.05 to 25)			

JBH492 total ADC (Cycle 3) n=2,0,3,5,2	1.96 (1 to 2.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter Tmax DM4 and sDM4

End point title	PK parameter Tmax DM4 and sDM4

End point description:

The time to reach maximum (peak) drug concentration (time) for DM4 and sDM4 based on splasma concentrations of DM4 and sDM4.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: hours				
median (full range (min-max))				
DM4 (Cycle 1)	2.08 (1.07 to 5.1)	2.03 (1.92 to 3.9)	1.18 (1.02 to 5.12)	2.05 (1 to 25)
DM4 (Cycle 3) n=2,0,3,5,2	2.08 (2.08 to 2.08)	999 (999 to 999)	1 (1 to 1.17)	2 (1.05 to 2.48)
sDM4 (Cycle 1)	281 (0 to 499)	163 (70.8 to 329)	71.8 (71.1 to 167)	72 (50.8 to 168)
sDM4 (Cycle 3) n=2,0,3,5,2	167 (166 to 167)	999 (999 to 999)	47.1 (46.4 to 47.7)	49 (22.1 to 71)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
median (full range (min-max))				
DM4 (Cycle 1)	1.18 (1 to 5.08)			
DM4 (Cycle 3) n=2,0,3,5,2	11.6 (1 to 22.2)			
sDM4 (Cycle 1)	37 (23.1 to 71.7)			

sDM4 (Cycle 3) n=2,0,3,5,2	59.5 (46.5 to 72.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter T1/2 JBH492 total antibody and JBH492 total ADC

End point title	PK parameter T1/2 JBH492 total antibody and JBH492 total ADC

End point description:

The elimination half-life associated with the terminal slope (λz) of a semi logarithmic concentration-time curve (time) for total antibody and total antibody-drug-conjugate based on serum concentrations of JBH492 total antibody and JBH492 total ADC.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: hours				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody (cycle1) n=1,0,2,0,1	39 (± 999)	999 (± 999)	91.4 (± 53.6)	999 (± 999)
JBH492 total ADC (cycle 1) n=4,3,5,7,6	84.8 (± 115.1)	87.9 (± 33.7)	89.3 (± 50.7)	109 (± 17.2)
JBH492 total ADC (cycle 3) n=1,0,1,5,2	150 (± 999)	999 (± 999)	80.1 (± 999)	145 (± 45.5)

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
geometric mean (geometric coefficient of variation)				
JBH492 total antibody (cycle1) n=1,0,2,0,1	214 (± 999)			
JBH492 total ADC (cycle 1) n=4,3,5,7,6	117 (± 21.4)			
JBH492 total ADC (cycle 3) n=1,0,1,5,2	164 (± 20.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter T1/2 DM4 and sDM4

End point title	PK parameter T1/2 DM4 and sDM4

End point description:

The elimination half-life associated with the terminal slope (λz) of a semi logarithmic concentration-time curve (time) for DM4 and sDM4 based on plasma concentrations of DM4 and sDM4.

Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1 and Cycle 3. One cycle=21 days.

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[22]	0[23]	2	5
Units: hours				
geometric mean (geometric coefficient of variation)				
DM4 (cycle 1) n=0,0,1,5,4	()	()	69.7 (± 999)	75 (± 25.5)
DM4 (cycle 3) n=0,0,0,5,2	()	()	999 (± 999)	142 (± 25.7)
sDM4 (cycle 1) n=0,0,2,0,2	()	()	173 (± 6.1)	999 (± 999)
sDM4 (cycle 3) n=0,0,0,2,2	()	()	999 (± 999)	181 (± 3.9)

Notes:

[22] - no participants with an available value for this endpoint

[23] - no participants with an available value for this endpoint

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hours				
geometric mean (geometric coefficient of variation)				
DM4 (cycle 1) n=0,0,1,5,4	104 (± 12.6)			
DM4 (cycle 3) n=0,0,0,5,2	158 (± 12.4)			
sDM4 (cycle 1) n=0,0,2,0,2	165 (± 9.1)			
sDM4 (cycle 3) n=0,0,0,2,2	197 (± 7.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-JBH492 antibodies

End point title	Incidence of anti-JBH492 antibodies

End point description:

Number of subjects with anti-JBH492 antibodies (Anti-Drug Antibodies)

End point type	Secondary

End point timeframe:

From baseline until last dose os study treatment up to approximately 1.5 years

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: participants				
ADA positive at baseline	0	0	2	1
ADA positive with study treatment	0	1	3	2

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: participants				
ADA positive at baseline	0			
ADA positive with study treatment	1			

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

On-treatment and post-treatment safety follow-up (FU) deaths were collected from first dose of study treatment to 157 days after last dose.
Survival FU deaths were collected from 157 days after last dose until end of study.
All deaths refer to the sum of pre-treatment deaths, on-treatment and post-treatment safety FU deaths,

and survival FU deaths.

End point type	Post-hoc

End point timeframe:

From first dose of study treatment up to over 157 days after last treatment
On-treatment and post-treatment safety FU deaths: up to approximately 1.6 years . Survival FU deaths: up to approximately 1.9 years

End point values	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	5	7
Units: participants				
On-treatment and post-treatment safety FU deaths	1	1	0	3
Survival FU deaths	0	0	0	0
All deaths	1	1	0	3

End point values	JHB492 3.6mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: participants				
On-treatment and post-treatment safety FU deaths	3			
Survival FU deaths	1			
All deaths	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events: from first dose of study treatment until 157 days after last treatment up to maximum duration of 1.6 years

Deaths: from first dose of study treatment until 157 days after last treatment up to maximum duration of 1.6 years

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	JBH492 0.4 mg/kg
Reporting group description: JBH492 0.4 mg/kg	
Reporting group title	JBH492 0.8 mg/kg
Reporting group description: JBH492 0.8 mg/kg	
Reporting group title	JBH492 1.6 mg/kg
Reporting group description: JBH492 1.6 mg/kg	
Reporting group title	JBH492 2.4 mg/kg
Reporting group description: JBH492 2.4 mg/kg	
Reporting group title	JBH492 3.6 mg/kg
Reporting group description: JBH492 3.6 mg/kg	
Reporting group title	All Subjects
Reporting group description: All Subjects	

Serious adverse events	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Autoimmune haemolytic anaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (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			
Extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (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	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (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			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (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 perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (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			
Calculus urinary			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (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
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (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
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (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

Serious adverse events	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg	All Subjects
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	4 / 6 (66.67%)	8 / 25 (32.00%)
number of deaths (all causes)	3	3	8
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Extravasation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			

subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	3 / 3 (100.00%)	5 / 5 (100.00%)
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	2 / 3 (66.67%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast			

disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema genital			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Scrotal oedema			
subjects affected / exposed	0 / 4 (0.00%)	2 / 3 (66.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Organising pneumonia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Stridor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	3
Activated partial thromboplastin time prolonged			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Amylase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 5 (40.00%)
occurrences (all)	1	0	2
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Prothrombin time prolonged			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Neutrophil count decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Keratorhexis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	3 / 5 (60.00%)
occurrences (all)	1	1	3
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	2 / 5 (40.00%)
occurrences (all)	0	2	3
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	2 / 5 (40.00%)
occurrences (all)	0	1	2
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Scleritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Punctate keratitis			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Corneal epithelial microcysts			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Urinary incontinence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ketosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tumour lysis syndrome			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg	All Subjects
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	5 / 6 (83.33%)	24 / 25 (96.00%)
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Extravasation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	3
Face oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	2	1	3
Mucosal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	1	0	4
Pain			

subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Oedema genital			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Scrotal oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	2
Organising pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Stridor			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 7 (28.57%)	3 / 6 (50.00%)	7 / 25 (28.00%)
occurrences (all)	4	4	11
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 7 (28.57%)	3 / 6 (50.00%)	7 / 25 (28.00%)
occurrences (all)	4	4	10
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	1	1	3
Blood bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Blood potassium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	5 / 25 (20.00%)
occurrences (all)	1	1	5
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	2	3
Lipase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Prothrombin time prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Platelet count decreased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	6	0	6
Injury, poisoning and procedural complications			
Keratorhexis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 6 (33.33%)	8 / 25 (32.00%)
occurrences (all)	1	2	8
Thrombocytopenia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 6 (16.67%)	6 / 25 (24.00%)
occurrences (all)	2	6	13
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	0	1	4
Leukopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	3
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Eye disorders			
Scleritis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Punctate keratitis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 6 (33.33%)	3 / 25 (12.00%)
occurrences (all)	0	2	3
Dry eye			
subjects affected / exposed	2 / 7 (28.57%)	2 / 6 (33.33%)	5 / 25 (20.00%)
occurrences (all)	2	2	5
Corneal epithelial microcysts			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	2	2
Conjunctival haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
Visual acuity reduced			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Ascites			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	1	1	3
Mouth ulceration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Eczema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Skin lesion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Skin ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 6 (33.33%)	2 / 25 (8.00%)
occurrences (all)	0	3	3

Neck pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 7 (28.57%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	2	0	2
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	3	0	3
Respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	2
Hypercalcaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Ketosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hypomagnesaemia			

subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
Tumour lysis syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 January 2020	Incorporated health authority feedback • Inclusion criteria updated to specify histologic subtypes of NHL permitted in the dose escalation part • Clarified inclusion criteria related to enrollment of patients with r/r CLL, r/r NHL, indolent lymphoma, Richter's transformation, and prior CAR-T therapy • Added recommendation for premedication to prevent IRRs in subsequent participants if early cohort participants experienced IRRs • Specified that in participants with grade 1 IRR, infusion rate to be decreased by 50% until recovery of symptoms to baseline • Added recommendations for the management of grade 2 and grade 3 IRRs and grade 3 and grade 4 tumor lysis syndrome • Definition of DLT updated; grade 4 hemolytic anemia, grade 4 thrombocytopenia, grade 3 skin rash, grade 2 pneumonitis, and grade 3 motor and/or sensory neuropathy were added as DLTs
01 August 2020	Incorporated health authority feedback • Clarified inclusion criteria related to relapsed or refractory disease, i.e., patients should have received and failed prior standard of care therapies and be intolerant or ineligible to approved therapies (conditions specified for CLL, NHL, and indolent lymphomas) • Inclusion criterion updated to add additional approved chemotherapeutics • Added ≥CTCAE grade 3 cytokine release syndrome as DLT • Added possibility of hospitalization up to 48 hours at Cycle 1 Day 1 in the dose escalation part, if required by health authority, to the Safety and tolerability section

30 November 2021	Updated exclusion criteria to allow patients with rapidly progressing NHL to be enrolled without unnecessary delay • Added exclusion criterion: patients who received any live vaccine against infectious diseases within 4 weeks prior to first dose of study treatment were not eligible • Added public health emergency mitigation procedures per updated regulation • Updated schedule of assessments to align with the section on ocular assessments where ophthalmologic exams during safety follow-up period if abnormal findings observed at EOT were included • For Japan only, change based on IB safety data: updated Japan hospitalization requirement from all of Cycle 1 to through C1D8 and included language for a longer stay based on general status of the participant • Updated schedule of assessments to clarify that lumbar puncture and CSF cytology were required at screening only for patients with CNS involvement or signs/symptoms of CNS involvement to reduce the burden of assessments for patients without CNS involvement • Specified that analysis of CCR7 expression may be performed on tumor material submitted from screen failure patients to utilize all samples collected in the escalation part, given that patient populations from the study selected indications are challenging to find • Aligned breastfeeding information with the IB: breast-feeding should not be performed while on study treatment, and for 180 days after discontinuation of JBH492 plus 60 days or five half-lives (whichever is longer) • Assessment of the benefit/risk concluded the absence of additional risks related to Covid-19 • Added physical exam for efficacy evaluations for NHL participants; physical exam would focus on assessment of constitutional symptoms as well as investigation of skin lesions • Multiple local clinical laboratory parameters were removed from collection because they are no longer required • Added HBV DNA to viral serology in local clinical laboratory parameters

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: