NOVARTIS

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

JBH942

Trial Indication(s)

Relapsed/refractory chronic lymphocytic leukemia (CLL)

Non-Hodgkin’s Lymphoma (NHL)

Protocol Number

CJBH492A12101

Protocol Title

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)

Clinical Trial Phase

Phase I/Ib

Phase of Drug Development

Phase I

NOVARTIS

Study Start/End Dates

Study Start Date: September 07, 2020 (Actual)
Primary Completion Date: September 05, 2024 (Actual)
Study Completion Date: September 05, 2024 (Actual)

Reason for Termination (If applicable)

Business, strategic, and development considerations and not due to any safety concerns

Study Design/Methodology

This was a first-in-human (FIH), open-label, Phase I/Ib, multi-center study that investigated JBH492 as a single agent and consisted of a dose escalation part, followed by an expansion part (the expansion part was not performed due to early study termination and not due to any safety reasons). The escalation part was conducted in participants with r/r CLL and r/r NHL. The study consisted of the following periods:

- Pre-treatment period: From the day of participants' first informed consent to the day before first administration of study treatment (Day −28 to Day −1).
- On-treatment period: From the date of first administration of study treatment (Day 1) to 30 days after the date of last actual administration of any study treatment (including start and stop dates).
- Post-treatment safety follow-up period (PTSFUP): Starting at Day 31 after the last administration of study treatment. All participants had safety follow up assessments 30, 60, 90, 120 and 150 days (+7-day window) after the last dose of study treatment.

Centers

8 centers in 7 countries: Germany(2), Korea, Republic of(1), Finland(1), Spain(1), Israel(1), Singapore(1), Japan(1)

Objectives:

Primary Objective

- 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

Secondary Objectives

- To evaluate the preliminary anti-tumor activity of single agent JBH492 in NHL
- To determine the pharmacokinetics (PK) of single agent JBH492, including total antibody (total Ab), total antibody-drug conjugate (ADC), DM4 (a maytansine-derived cytotoxic payload), and S-Methyl DM4 (S-Methyl DM4 is also known as DM4-Me and is hereafter referred to as DM4-Me in the report)
- To assess the immunogenicity (IG) of JBH492

Test Product (s), Dose(s), and Mode(s) of Administration

Lyophilisate powder for intravenous injection every 3 weeks at 0.4, 0.8, 1.6, 2.4 or 3.6 mg/kg.

Statistical Methods

Maximum Tolerated Dose/Recommended Dose

Dose-limiting toxicities

Estimation of the MTD of the treatment was planned to be based upon the estimation of the probability of DLT in Cycle 1 (i.e., the first 21 days) for participants in the DDS. A recommended dose below the MTD could be identified based on other safety, clinical, PK, and PD data.

BHLRM with EWOC approach

The relationship between dose and the probability of DLT was modelled using Bayesian Hierarchical Logistic Regression Model (BHLRM) for single-agent JBH492 based on the DDS. DLT data from two different disease areas, NHL and CLL, were combined using a Bayesian hierarchical structure. BHLRM with Escalation With Overdose Control (EWOC) principle was used to make dosing decisions. A dose could only be used for newly enrolled participants if the risk of excessive toxicity at that dose was less than 25%.

Assessment of participant risk

After each cohort of participants in dose escalation, the posterior distribution for the risk of DLT for new participants at doses of interest were evaluated. The posterior distributions were summarized to provide the posterior probability that the risk of DLT lies within the following intervals:

Under-dosing: [0, 0.16)

Targeted toxicity: [0.16, 0.33)

Excessive toxicity: [0.33, 1]

The MTD was defined as the highest dose estimated to have less than 25% risk of causing a DLT during the DLT evaluation period in more than 33% of treated participants.

The MTD declaration was to occur when the following conditions were met:

- At least 6 treated participants at the dose to be determined as the MTD
- This dose satisfied one of the following conditions:

(1) The posterior probability of targeted toxicity at this dose exceeded 50% and was the highest among the potential doses, or

(2) Minimum of 21 treated participants on the trial if the escalation is always joint for NHL and CLL; minimum of 14 treated participants per disease area if the escalation is separated per the BHLRM model recommendation.

Safety, tolerability, efficacy, and PK

Data were summarized using descriptive statistics (continuous data) and/or contingency tables (categorical data) for demographic and baseline characteristics, efficacy measurements, safety measurements, and all relevant PK and PD measurements.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

For patients with CLL:

• Confirmed diagnosis of chronic lymphocytic leukemia (CLL)

For patients with NHL:

• Histologically confirmed diagnosis of B- or T-cell non-Hodgkins lymphoma (NHL).

• Must have a site of disease amenable to biopsy, and be suitable and willing to undergo study required biopsies at screening and during therapy.

Exclusion Criteria, applicable to both CLL and NHL:

• History of anaphylactic or other severe hypersensitivity/infusion reactions to ADCs, monoclonal antibodies (mAbs) and/or their excipients such that the patient in unable to tolerate immunoglobulin/monoclonal antibody administration

• Any prior history of treatment with maytansine (DM1 or DM4)-based ADC

• Known intolerance to a maytansinoid

• Patients with any active or chronic corneal disorders

• Patients who have any other condition that precludes monitoring of the retina or fundus

• Patients with active CNS involvement are excluded, except if the CNS involvement has been effectively treated and provided that

local treatment was completed >4 weeks before first dose of study treatment. Patients that have been effectively treated for CNS disease and are stable under systemic therapy may be enrolled provided all other inclusion and exclusion criteria are met. Patients who received prophylactic intrathecal treatment are eligible, if treatment discontinued >5 half-lives prior to the first dose of study treatment

• Impaired cardiac function or clinically significant cardiac disease

• Known history of Human Immunodeficiency Virus (HIV) infection

• Active HBV or HCV infection. Patients whose disease is controlled under antiviral therapy should not be excluded. Patients who are anti-HBcAb positive should be HBsAg negative and HBV-DNA negative to be eligible

Other inclusion and exclusion criteria may apply.

Participant Flow Table

Overall Study

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4mg/kg	JHB492 3.6mg/kg	Total
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks	
Started	4	3	5	7	6	25
Completed	0	0	0	0	0	0
Not Completed	4	3	5	7	6	25
Adverse Event	0	0	0	0	2	2
Death	1	0	0	1	0	2
Progressive disease	3	3	5	6	3	20

Participant decision	0	0	0	0	1	1

Baseline Characteristics

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg	Total
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks	
Number of Participants [units: participants]	4	3	5	7	6	25
Baseline Analysis Population Description						
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation						
	75±9.06	71±3.61	64.4±10.36	65.1±10.09	59.5±13.81	65.9±11.06
Age, Customized (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)						
18 - < 65 years	1	0	2	3	4	10
65 - < 85 years	2	3	3	4	2	14
>= 85 years	1	0	0	0	0	1
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)						

Female	2	0	1	3	2	8
Male	2	3	4	4	4	17
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)						
American Indian or Alaska Native	0	0	0	0	0	0
Asian	1	1	2	1	1	6
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0
Black or African American	0	0	0	1	1	2
White	3	2	3	5	4	17
More than one race	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0

Primary Outcome Result(s)

Number of participants with dose limiting toxicities (DLTs)

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
Time Frame	First cycle of treatment (21 days)
Analysis Population Description	Dose determining set (DDS): includes all FAS subjects (i.e. who received at least one dose of JBH492) who have sufficient safety evaluations (as determined by Novartis and Investigator), or experienced a dose limiting toxicity (DLT) during the DLT-evaluation period, i.e. 21 days of dosing.

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	3	3	5	7	5
Number of participants with dose limiting toxicities (DLTs) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
All Grades	0 (%)	0 (%)	1 (20%)	0 (%)	0 (%)

Number of participants with on treatment Adverse Events (AEs)

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
Time Frame	rom treatment day 1 until 30 days post last treatment up to approximately 1.6 years
Analysis Population Description	Safety Set (SS) comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6

Number of participants with on treatment Adverse Events (AEs) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
AEs	4 (100%)	3 (100%)	5 (100%)	7 (100%)	5 (83.33%)
AEs suspected to be treatment related	1 (25%)	1 (33.33%)	3 (60%)	6 (85.71%)	5 (83.33%)
AEs requiring additional therapy	3 (75%)	2 (66.67%)	3 (60%)	5 (71.43%)	5 (83.33%)

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

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.
Time Frame	From treatment day 1 until 30 days post last treatment up to approximately 1.6 years
Analysis Population Description	Safety Set (SS) comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
Number of participants with on treatment Serious Adverse Events (SAEs) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
SAEs	1 (25%)	1 (33.33%)	0 (%)	2 (28.57%)	3 (50%)

SAEs suspected to be treatment related	0 (%)	0 (%)	0 (%)	0 (%)	2 (33.33%)

Number of participants with dose interruptions and dose reductions

Description	Tolerability measured by the number of subjects who have interruptions or reductions of study treatment
Time Frame	From first dose of study treatment until last dose up to approximately 1.5 years
Analysis Population Description	Safety Set (SS) comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
Number of participants with dose interruptions and dose reductions (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Participants with at least one dose reduction or interruption	0 (%)	0 (%)	0 (%)	3 (42.86%)	2 (33.33%)
Participants with at least one dose reduction	0 (%)	0 (%)	0 (%)	1 (14.29%)	2 (33.33%)
Participants with at least one dose interruption	0 (%)	0 (%)	0 (%)	2 (28.57%)	0 (%)

Cumulative dose

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.

Time Frame	From first dose of study treatment until last dose up to approximately 1.5 years
Analysis Population Description	Safety Set (SS) comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
Cumulative dose (units: mg/Kg)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	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)	7.20 (3.6 to 57.6)

Relative dose intensity

Description	Tolerability measured by the 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
Time Frame	From baseline until last dose os study treatment up to approximately 1.5 years
Analysis Population Description	Safety Set (SS) comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks

Number of Participants Analyzed [units: participants]	4	3	5	7	6
Relative dose intensity (units: Ratio)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	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)	1.000 (1.00 to 1.00)

Secondary Outcome Result(s)

Best overall response (BOR) in CLL participants

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).
Time Frame	From baseline up to 157 days after last dose
Analysis Population Description	Participants in the full analysis set (FAS) with CLL. The FAS comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	0	0	1	0	0
Best overall response (BOR) in CLL participants (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Progressive Disease	(NaN%)	(NaN%)	1 (100%)	(NaN%)	(NaN%)

NOVARTIS

Best overall response (BOR) in NHL participants

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.
Time Frame	From baseline up to 157 days after last dose
Analysis Population Description	Participants in the full analysis set (FAS) with NHL. The FAS comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	4	7	6
Best overall response (BOR) in NHL participants (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Complete Response (CR)	0 (%)	0 (%)	0 (%)	0 (%)	1 (16.67%)
Partial Response (PR)	0 (%)	0 (%)	0 (%)	3 (42.86%)	1 (16.67%)
Stable Disease	0 (%)	0 (%)	1 (25%)	0 (%)	0 (%)
Progressive Disease	3 (75%)	3 (100%)	3 (75%)	4 (57.14%)	3 (50%)
Unkown	1 (25%)	0 (%)	0 (%)	0 (%)	1 (16.67%)

Overall response rate (ORR) in NHL participants

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.
Time Frame	From baseline up to 157 days after last dose
Analysis Population Description	Participants in the full analysis set (FAS) with NHL. The FAS comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	4	7	6
Overall response rate (ORR) in NHL participants (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	0 (%)	0 (%)	0 (%)	3 (42.86%)	2 (33.33%)

Duration of Response (DOR) in NHL participants

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.
Time Frame	From baseline up to 157 days after last dose
Analysis Population Description	Participants in the full analysis set (FAS) with NHL and complete or partial response. The FAS comprises all subjects who received at least one dose of JBH492

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	0	0	0	3	2
Duration of Response (DOR) in NHL participants (units: Months)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
				NA ± NA[1]	NA ± NA[1]

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

Progression Free Survival (PFS) in NHL participants

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.
Time Frame	From baseline up to 157 days after last dose
Analysis Population Description	Participants in the full analysis set (FAS) with NHL. The FAS comprises all subjects who received at least one dose of JBH492

	Low dose JBH492 0.4/0.8/1.6 mg/kg	High dose JBH492 2.4/3.6 mg/kg
Arm/Group Description	JBH492 0.4, 0.8 and 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 and 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	11	13
Progression Free Survival (PFS) in NHL participants (units: Months)	**Median (Inter-Quartile Range)**	**Median (Inter-Quartile Range)**
	1.0 (0.7 to 1.9)	2.1 (2.1 to 8.9)

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

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
Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
Pharmacokinetics (PK) parameter AUClast JBH492 total antibody and JBH492 total ADC (units: hours * ug/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
JBH492 total antibody (cycle 1)	1080 (57.6%)	1460 (18.0%)	4450 (36.4%)	9330 (35.6%)	9300 (99.6%)
JBH492 total antibody (cycle 3)	1320 (0.8%)		3290 (255.2%)	17600 (31.8%)	20600 (38.3%)
JBH492 antibody- drug conjugate (cycle 1)	598 (38.7%)	822 (41.1%)	2280 (18.1%)	5590 (29.0%)	6030 (53.6%)
JBH492 antibody- drug conjugate (cycle 3)	434 (20.4%)		1440 (61.9%)	5630 (21.5%)	7090 (28.0%)

Pharmacokinetics (PK) parameter AUClast DM4 and sDM4

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.

Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
Pharmacokinetics (PK) parameter AUClast DM4 and sDM4 (units: hours * ug/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
DM4 (cycle 1)	4.86 (195.2%)	14.6 (35.8%)	77.9 (23.1%)	142 (23.6%)	177 (48.2%)
DM4 (cycle 3)	11.8 (5.8%)		47.2 (30.3%)	231 (41.3%)	248 (16.2%)
sDM4 (Cycle 1)	54.1 (15.4%)	135 (32.1%)	547 (43.9%)	435 (52.4%)	332 (348.2%)
sDM4 (Cycle 3)	154 (10.1%)		522 (378.6%)	784 (64.7%)	562 (86.1%)

PK parameter AUCinf JBH492 total antibody and JBH492 total ADC

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.
Time Frame	pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1. One cycle=21 days.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	5
PK parameter AUCinf JBH492 total antibody and JBH492 total ADC (units: hour*ug/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
JBH942 total antibody	489		3700 (66.2%)		17500
JBH942total antibody-drug-conjugate	643 (36.1%)	900 (32.9%)	2380 (17.6%)	5900 (29.9%)	7660 (19.8%)

PK parameter AUCinf DM4 and sDM4

Description	The AUC from time zero to infinity (mass × time × volume-1) for DM4 and sDM4 based on plasma concentrations of DM4 and sDM4.
Time Frame	pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 1. One cycle=21 days.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	0	0	2	5	4
PK parameter AUCinf DM4 and sDM4 (units: hour*ug/mL)	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**

	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)
DM4			94.4	158 (23.6%)	226 (25.0%)
sDM4			614 (17.1%)		601 (70.6%)

PK parameter AUCtau JBH492 total antibody and JBH492 total ADC

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.
Time Frame	Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 3. One cycle=21 days
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	1	0	1	5	2
PK parameter AUCtau JBH492 total antibody and JBH492 total ADC (units: hour*ug/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
JBH492 total antibody					
JBH492 total antibody-drug-conjugate	547		2650	5730 (21.4%)	7100 (28%)

PK parameter AUCtau DM4 and sDM4

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.
Time Frame	Pre-dose, 1, 4, 24, 48, 72, 168, 336 and 504 hours post-dose on Day 1 of Cycle 3. One cycle=21 days
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	0	0	0	5	2
PK parameter AUCtau DM4 and sDM4 (units: hour*ug/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
DM4				239 (40.3%)	248 (16.2%)
sDM4				1100 (76.9%)	563 (86.1%)

PK parameter Cmax JBH492 total antibody and JBH492 total ADC

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.
Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
PK parameter Cmax JBH492 total antibody and JBH492 total ADC (units: ug/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**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%)	56.1 (19.0%)
JBH492 total antibody (Cycle 3)	6.8 (28.2%)		30.3 (17.6%)	71.7 (14.3%)	65.2 (49.5%)
JBH492 total antibody-drug-conjugate (Cycle 1)	7.03 (30.9%)	7.81 (74.2%)	27.2 (11.5%)	49.4 (17.5%)	66.4 (22.0%)
JBH492 total antibody-drug-conjugate (Cycle 3)	5.11 (37.8%)		24.8 (19.4%)	53.8 (15.3%)	53.2 (17.6%)

PK parameter Cmax DM4 and sDM4

Description	The maximum (peak)observed serum drug concentration (mass × volume-1) for DM4 and sDM4 based on plasma concentrations of DM4 and sDM4.
Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks

Number of Participants Analyzed [units: participants]	4	3	5	7	6
PK parameter Cmax DM4 and sDM4 (units: ug/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**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%)	2.48 (42.7%)
DM4 (Cycle 3)	0.305 (6.7%)		2.05 (238.8%)	4.91 (320.2%)	2.43 (37.2%)
sDM4 (Cycle 1)	0.196 (26.1%)	0.567 (25.0%)	2.01 (24.9%)	1.64 (53.9%)	2.19 (55.6%)
sDM4 (Cycle 3)	0.522 (9.4%)		4.62 (70.0%)	3.32 (65.9%)	2.46 (84.7%)

PK parameter Tmax JBH492 total antibody and JBH492 total ADC

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.
Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
PK parameter Tmax JBH492 total antibody and JBH492 total ADC (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**

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)	2.95 (1 to 5)
JBH492 total antibody (Cycle 3)	86 (4.88 to 167)		3.92 (1.17 to 4)	2 (1.05 to 2.48)	11.6 (1 to 22.2)
JBH492 total antibody-drug-conjugate (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)	4.05 (1.05 to 25)
JBH492 total antibody-drug-conjugate (Cycle 3)	25.4 (2.08 to 48.6)		3.92 (1.17 to 4)	2.48 (1.05 to 5.08)	1.96 (1 to 2.92)

PK parameter Tmax DM4 and sDM4

Description	The time to reach maximum (peak) drug concentration (time) for DM4 and sDM4 based on splasma concentrations of DM4 and sDM4.
Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
PK parameter Tmax DM4 and sDM4 (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
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)	1.18 (1 to 5.08)
DM4 (Cycle 3)	2.08 (2.08 to 2.08)		1 (1 to 1.17)	2 (1.05 to 2.48)	11.6 (1 to 22.2)
sDM4 (Cycle 1)	281 (0 to 499)	163 (70.8 to 329)	71.8 (71.1 to 167)	72 (50.8 to 168)	37 (23.1 to 71.7)

sDM4 (Cycle 3)	167 (166 to 167)	47.1 (46.4 to 47.7)	49 (22.1 to 71)	59.5 (46.5 to 72.5)

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

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.
Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
PK parameter T1/2 JBH492 total antibody and JBH492 total ADC (units: hours)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
JBH492 total antibody (cycle1)	39		91.4 (53.6%)		214
JBH492 antibody-drug-conjugate (cycle 1)	84.8 (115.1%)	87.9 (33.7%)	89.3 (50.7%)	109 (17.2%)	117 (21.4%)
JBH492 antibody-drug-conjugate (cycle 3)	150		80.1	145 (45.5%)	164 (20.2%)

PK parameter T1/2 DM4 and sDM4

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.
Time Frame	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.
Analysis Population Description	Participants in the Pharmacokinetic analysis set (PAS) with and available value for the outcome measure. The PAS included all participants who provided an evaluable PK profile. A profile was considered evaluable if the participant received one dose of JBH492 and provided at least one PK parameter.

	JBH492 0.4 mg/kg	**JBH492 0.8 mg/kg**	**JBH492 1.6mg/kg**	**JBH492 2.4 mg/kg**	**JBH492 3.6 mg/kg**
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	0	0	2	5	4
PK parameter T1/2 DM4 and sDM4 (units: hours)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
DM4 (cycle 1)			69.7	75 (25.5%)	104 (12.6%)
DM4 (cycle 3)				142 (25.7%)	158 (12.4%)
sDM4 (cycle 1)			173 (6.1%)		165 (9.1%)
sDM4 (cycle 3)				181 (3.9%)	197 (7.3%)

Incidence of anti-JBH492 antibodies

Description	Number of subjects with anti-JBH492 antibodies (Anti-Drug Antibodies)
Time Frame	From baseline until last dose os study treatment up to approximately 1.5 years

Analysis Population Description	The immunogenicity incidence set (IGIS) includes all participants in the safety set with with a non-missing baseline ADA sample and at least one non-missing post-baseline ADA sample. Safety set (SS) comprised all participants who received at least one dose of JBH492

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	5
Incidence of anti-JBH492 antibodies (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
ADA positive at baseline	0 (%)	0 (%)	2 (40%)	1 (14.29%)	0 (%)
ADA positive with study treatment	0 (%)	1 (33.33%)	3 (60%)	2 (28.57%)	1 (20%)

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

All collected deaths

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.
Time Frame	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

Analysis Population Description

	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg intravenously once every 3 weeks	JBH492 2.4 mg/kg intravenously once every 3 weeks	JBH492 3.6 mg/kg intravenously once every 3 weeks
Number of Participants Analyzed [units: participants]	4	3	5	7	6
All collected deaths (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
On-treatment and post-treatment safety FU deaths	1 (25%)	1 (33.33%)	0 (%)	3 (42.86%)	3 (50%)
Survival FU deaths	0 (%)	0 (%)	0 (%)	0 (%)	1 (16.67%)
All deaths	1 (25%)	1 (33.33%)	0 (%)	3 (42.86%)	4 (66.67%)

Safety Results

Time Frame	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
Source Vocabulary for Table Default	MedDRA (27.0)

Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	JBH492 0.4 mg/kg N = 4	JBH492 0.8 mg/kg N = 3	JBH492 1.6 mg/kg N = 5	JBH492 2.4 mg/kg N = 7	JBH492 3.6 mg/kg N = 6	All Subjects N = 25
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg intravenously once every 3 weeks	All Subjects
Total Number Affected	1	1	0	3	3	8
Total Number At Risk	4	3	5	7	6	25

Serious Adverse Events

Time Frame	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
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

	JBH492 0.4 mg/kg N = 4	JBH492 0.8 mg/kg N = 3	JBH492 1.6 mg/kg N = 5	JBH492 2.4 mg/kg N = 7	JBH492 3.6 mg/kg N = 6	All Subjects N = 25
Arm/Group Description	JBH492 0.4 mg/kg intravenously once every 3 weeks	JBH492 0.8 mg/kg intravenously once every 3 weeks	JBH492 1.6 mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg intravenously once every 3 weeks	All Subjects
Total # Affected by any Serious Adverse Event	1	1	0	2	4	8
Total # at Risk by any Serious Adverse Event	4	3	5	7	6	25
Blood and lymphatic system disorders						
Autoimmune haemolytic anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Eye disorders						
Vision blurred	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Gastrointestinal disorders						
Intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Intestinal perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
General disorders and administration site conditions						
Extravasation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
General physical health deterioration	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Immune system disorders						
Haemophagocytic lymphohistiocytosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)

Infections and infestations						
Abdominal sepsis	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Device related infection	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Renal and urinary disorders						
Calculus urinary	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)

Other (Not Including Serious) Adverse Events

Time Frame	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
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	JBH492 0.4 mg/kg N = 4	**JBH492 0.8 mg/kg N = 3**	**JBH492 1.6 mg/kg N = 5**	**JBH492 2.4 mg/kg N = 7**	**JBH492 3.6 mg/kg N = 6**	**All Subjects N = 25**
Arm/Group Description	JBH492 0.4 mg/kg	JBH492 0.8 mg/kg	JBH492 1.6 mg/kg	JBH492 2.4 mg/kg	JBH492 3.6 mg/kg	All Subjects

	intravenously once every 3 weeks	intravenously once every 3 weeks			intravenously once every 3 weeks	
Total # Affected by any Other Adverse Event	4	3	5	7	5	24
Total # at Risk by any Other Adverse Event	4	3	5	7	6	25
Blood and lymphatic system disorders						
Anaemia	1 (25.00%)	1 (33.33%)	3 (60.00%)	1 (14.29%)	2 (33.33%)	8 (32.00%)
Autoimmune haemolytic anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Leukopenia	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (14.29%)	0 (0.00%)	2 (8.00%)
Neutropenia	0 (0.00%)	1 (33.33%)	2 (40.00%)	0 (0.00%)	1 (16.67%)	4 (16.00%)
Thrombocytopenia	0 (0.00%)	1 (33.33%)	2 (40.00%)	2 (28.57%)	1 (16.67%)	6 (24.00%)
Ear and labyrinth disorders						
Deafness	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Eye disorders						
Conjunctival haemorrhage	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Corneal epithelial microcysts	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Dry eye	1 (25.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	2 (33.33%)	5 (20.00%)
Punctate keratitis	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	3 (12.00%)
Scleritis	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Vision blurred	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (16.67%)	2 (8.00%)
Visual acuity reduced	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (16.67%)	2 (8.00%)
Gastrointestinal disorders						
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)

Ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Constipation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Diarrhoea	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (14.29%)	1 (16.67%)	3 (12.00%)
Mouth ulceration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
General disorders and administration site conditions						
Asthenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	1 (16.67%)	3 (12.00%)
Extravasation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Face oedema	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Fatigue	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	2 (8.00%)
Generalised oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Mucosal inflammation	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Oedema peripheral	0 (0.00%)	2 (66.67%)	1 (20.00%)	1 (14.29%)	0 (0.00%)	4 (16.00%)
Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Immune system disorders						
Cytokine release syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Infections and infestations						
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	0 (0.00%)	2 (8.00%)
Cytomegalovirus chorioretinitis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Infection	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Urinary tract infection	0 (0.00%)	1 (33.33%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	2 (8.00%)
Injury, poisoning and procedural complications						

Keratorhexis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Investigations						
Activated partial thromboplastin time prolonged	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	2 (40.00%)	2 (28.57%)	3 (50.00%)	7 (28.00%)
Amylase increased	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	2 (40.00%)	2 (28.57%)	3 (50.00%)	7 (28.00%)
Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (14.29%)	1 (16.67%)	3 (12.00%)
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (16.67%)	2 (8.00%)
Blood lactate dehydrogenase increased	1 (25.00%)	0 (0.00%)	2 (40.00%)	1 (14.29%)	1 (16.67%)	5 (20.00%)
Blood potassium decreased	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Lipase increased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Platelet count decreased	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	2 (8.00%)
Prothrombin time prolonged	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Metabolism and nutrition disorders						
Hypercalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Hypokalaemia	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	2 (8.00%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (16.67%)	2 (8.00%)
Hypophosphataemia	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Ketosis	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Tumour lysis syndrome	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)

Musculoskeletal and connective tissue disorders						
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	2 (8.00%)
Neck pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Nervous system disorders						
Migraine	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Psychiatric disorders						
Mental status changes	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Renal and urinary disorders						
Acute kidney injury	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Pollakiuria	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Urinary incontinence	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Reproductive system and breast disorders						
Erectile dysfunction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)
Oedema genital	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Scrotal oedema	0 (0.00%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (8.00%)
Respiratory, thoracic and mediastinal disorders						
Cough	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Dyspnoea	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Nasal congestion	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	2 (8.00%)
Organising pneumonia	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Stridor	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Skin and subcutaneous tissue disorders						

Dry skin	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Eczema	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Pruritus	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (14.29%)	0 (0.00%)	2 (8.00%)
Rash	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Rash maculo-papular	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (4.00%)
Skin lesion	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Skin ulcer	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.00%)
Vascular disorders						
Venous thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (4.00%)

Other Relevant Findings

N/A

Conclusion:

- The FIH study of JBH492 in participants with r/r CLL and r/r NHL demonstrated an approximate dose-dependent increase in PK parameters (Cmax and AUClast) for JBH492 antibody.
- Overall, results from the dose escalation part of the study indicate an acceptable and manageable safety profile of JBH492. The dose of 2.4 mg/kg Q3W was regarded to be promising, based on available safety, PK, and efficacy data, and provides a basis for further clinical evaluation.
- The high rate of study treatment discontinuation due to rapidly progressive disease highlights the predominantly heavily pretreated patient population with r/r CLL and r/r NHL enrolled in this study. Nevertheless, a modest efficacy signal was observed in the NHL population with an ORR of 20.8% across all doses evaluated.

- The observed immunogenicity profile suggests that JBH492 induces an immune response, which may impact its long-term safety and efficacy. Further studies are warranted to better understand the PK, immunogenicity, safety, and efficacy of JBH492.

Date of Clinical Trial Report

27 March 2025 (date of Published CSR)