



Clinical trial results:

A Phase IIa, Open-label, Multicenter Study of Single-agent MOR00208, an Fc-Optimized Anti-CD19 Antibody, in Patients with Relapsed or Refractory B-Cell Non-Hodgkin's Lymphoma

Summary

EudraCT number	2012-002659-41
Trial protocol	BE IT HU ES DE PL
Global end of trial date	06 April 2022

Results information

Result version number	v2 (current)
This version publication date	21 April 2023
First version publication date	05 January 2019
Version creation reason	• New data added to full data set Availability of final CSR

Trial information

Trial identification

Sponsor protocol code	MOR208C201
-----------------------	------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01685008
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Morphosys AG
Sponsor organisation address	Semmelweisstrasse 7, Planegg, Germany, 82152
Public contact	Medical Information, Morphosys AG, +1 844 667-1992, medinfo@morphosys.com
Scientific contact	Medical Information, Morphosys AG, +1 844 667-1992, medinfo@morphosys.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	15 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 April 2022
Global end of trial reached?	Yes
Global end of trial date	06 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the antitumor activity of single-agent MOR00208 in adult patients with relapsed or refractory NHL who have received at least 1 prior therapy containing rituximab as one of the treatments.

Protection of trial subjects:

This trial was designed, conducted and reported in accordance with the International Conference on Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP), applicable local regulations (including European Directive 2001/20/EC), and following the ethical principles laid down in the Declaration of Helsinki. Specific ICH adopted and other relevant international guidelines and recommendations were taken into account as far as meaningfully possible. Safety monitoring for all patients enrolled in the study included laboratory safety assessments (haematology, blood chemistry, urinalysis, coagulation, and anti-MOR00208 antibodies) and clinical evaluations (physical examinations, vital signs, 12-lead ECG) as detailed in the Schedule of Assessments.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 April 2013
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	Spain: 12
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Poland: 16
Worldwide total number of subjects	92
EEA total number of subjects	72

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	43
From 65 to 84 years	46
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

This was a Phase IIa open-label, multicenter safety and efficacy study of MOR00208, that was planned to enroll approximately 40 to 120 adult patients with refractory or relapsed NHL who have received at least 1 prior therapy containing rituximab.

Pre-assignment

Screening details:

Patients were male or female ≥ 18 years of age, with a histologically confirmed diagnosis of FL, other indolent NHL (e.g., MZL/MALT), DLBCL, or MCL. Patients must have had progression of their NHL after at least 1 prior rituximab-containing regimen, and had at least 1 site of measurable disease on an MRI or CT scan.

Period 1

Period 1 title	Screening Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	MOR00208
-----------	----------

Arm description:

A total of 113 patients were screened; of these, 21 were screening failures and did not receive treatment with MOR00208. 92 patients completed screening and received at least one dose of study drug.

Arm type	Experimental
Investigational medicinal product name	MOR00208
Investigational medicinal product code	MOR00208
Other name	MOR208, XmAb5574, tafasitamab
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use

Dosage and administration details:

MOR00208 drug product is a lyophilisate supplied in single-use 20 mL glass vials. Each vial contains 200 mg of MOR00208 for reconstitution with 5 mL water for injection. Intravenous infusions were administered at the study site, beginning on Cycle 1 Day 1.

Number of subjects in period 1	MOR00208
Started	92
Completed	92

Period 2

Period 2 title	Main Study Treatment (Cycles 1-2)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	MOR00208
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MOR00208
Investigational medicinal product code	MOR00208
Other name	MOR208, XmaB5574, tafasitamab
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use

Dosage and administration details:

MOR00208 drug product is a lyophilisate supplied in single-use 20 mL glass vials. Each vial contains 200 mg of MOR00208 for reconstitution with 5 mL water for injection. Intravenous infusions were administered at the study site, beginning on Cycle 1 Day 1.

Number of subjects in period 2	MOR00208
Started	92
Completed	75
Not completed	17
Adverse event, serious fatal	4
Physician decision	2
Adverse event, non-fatal	3
Progressive disease	7
Protocol deviation	1

Period 3

Period 3 title	Post Cycle 2 (C3 and Maintenance)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	MOR00208
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	MOR00208
Investigational medicinal product code	MOR00208
Other name	MOR208, XmAb5574, tafasitamab
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use

Dosage and administration details:

MOR00208 drug product is a lyophilisate supplied in single-use 20 mL glass vials. Each vial contains 200 mg of MOR00208 for reconstitution with 5 mL water for injection. Intravenous infusions were administered at the study site, beginning on Cycle 1 Day 1.

Number of subjects in period 3	MOR00208
Started	75
Started Cycle 3 Treatment	50
Started Maintenance Phase Treatment	16
Completed	1
Not completed	74
Adverse event, serious fatal	1
Consent withdrawn by subject	4
Physician decision	10
Other	5
New cancer therapy	7
Unspecified	1
Progressive disease	46

Baseline characteristics

Reporting groups

Reporting group title	MOR00208
-----------------------	----------

Reporting group description:

A total of 113 patients were screened; of these, 21 were screening failures and did not receive treatment with MOR00208. 92 patients completed screening and received at least one dose of study drug.

Reporting group values	MOR00208	Total	
Number of subjects	92	92	
Age categorical			
Age (years)			
Units: Subjects			
Adults (18-64 Years)	43	43	
Adults (65 and over)	49	49	
Age continuous			
Age mean and SD			
Units: years			
arithmetic mean	65.57		
standard deviation	± 12.225	-	
Gender categorical			
Units: Subjects			
Female	36	36	
Male	56	56	
Race			
Units: Subjects			
Asian	1	1	
Black or African American	1	1	
White	87	87	
Other	3	3	
NHL Subtype			
Units: Subjects			
Follicular lymphoma	34	34	
Diffuse large B-cell lymphoma	35	35	
Mantle cell lymphoma	12	12	
Other indolent NHL	11	11	
Weight			
Units: kg			
arithmetic mean	77.10		
standard deviation	± 17.012	-	
Height			
n=90 for this characteristic, as height was not collected at Screening (minor protocol noncompliance) for 2 patients in the Safety Population.			
Units: cm			
arithmetic mean	169.30		
standard deviation	± 11.954	-	
BMI			
n=90 for this characteristic, as height was not collected at Screening (minor protocol noncompliance) for 2 patients in the Safety Population.			

Units: kg/m2			
arithmetic mean	26.86		
standard deviation	± 5.133	-	

End points

End points reporting groups

Reporting group title	MOR00208
Reporting group description: A total of 113 patients were screened; of these, 21 were screening failures and did not receive treatment with MOR00208. 92 patients completed screening and received at least one dose of study drug.	
Reporting group title	MOR00208
Reporting group description: -	
Reporting group title	MOR00208
Reporting group description: -	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR) ^[1]
End point description: Proportion of Patients with Complete Remission (CR) or Partial Remission (PR), assessed as per the 2007 International Working Group (IWG) response criteria	
End point type	Primary
End point timeframe: From first dose until Follow-up Visit 12, up to 4.5 years	

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: The primary endpoint for this open-label study was a count of responders; no statistical analyses or comparisons are applicable.

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: patients				
Complete remission	6			
Partial remission	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Stable Disease (SD) Rate

End point title	Stable Disease (SD) Rate
End point description: Proportion of Patients with Stable Disease	
End point type	Secondary
End point timeframe: From first dose until Follow-up Visit 12, up to 4.5 years	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: patients	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)
End point description: Time from first response (CR or PR) to first documentation of relapse/progression, for patients who had any response during the study.	
End point type	Secondary
End point timeframe: From first dose until Follow-up Visit 12, up to 4.5 years	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	22 ^[2]			
Units: Months				
median (confidence interval 95%)	24.0 (11.1 to 1000000)			

Notes:

[2] - The upper CI was not reached; "1000000" entered as numerical value required.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)
End point description: Time from first dosing until documentation of progression or death due to lymphoma	
End point type	Secondary
End point timeframe: From first dose until Follow-up Visit 12, up to 4.5 years	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	76 ^[3]			
Units: Months				
median (confidence interval 95%)	5.4 (3.4 to 12.0)			

Notes:

[3] - Patients with documented progression of disease.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
End point description:	
Time from first dosing until progression or death due to any cause	
End point type	Secondary
End point timeframe:	
From first dose until Follow-up Visit 12, up to 4.5 years	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	80 ^[4]			
Units: Months				
median (confidence interval 95%)	5.4 (3.2 to 9.9)			

Notes:

[4] - Patients with documented progression or death from any cause.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and Severity of Adverse Events (AEs)

End point title	Incidence and Severity of Adverse Events (AEs)
End point description:	
Number of patients with treatment-emergent AEs rated Mild, Moderate, and Severe	
End point type	Secondary
End point timeframe:	
From first dose until 30 days after last dose of MOR00208, up to 8.5 years	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: patients				
Mild	29			
Moderate	20			
Severe	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number and Proportion of Patients Who Potentially Developed Anti-MOR00208 Antibodies and Semiquantitative Anti-MOR00208 Antibody Assessments

End point title	Number and Proportion of Patients Who Potentially Developed Anti-MOR00208 Antibodies and Semiquantitative Anti-MOR00208 Antibody Assessments
-----------------	--

End point description:

Number of patients with at least one positive (+ve) post-Baseline sample containing positive anti-MOR00208 antibodies; Baseline (pre-dose) sample has to be tested negative (-ve)

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

End point timeframe:

From first dose until Follow-up Visit 3, up to 7 months

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: patients				
Yes (≥ 1 +ve sample post-Baseline inc last sample)	0			
No (Baseline and all post-Baseline samples -ve)	82			
Transient (≥ 1 +ve post-Baseline, -ve last sample)	0			
Not evaluable (pre-dose sample tested +ve)	5			
Missing (no post-Baseline measurement available)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: Maximum Serum Concentration Observed (Cmax) of MOR00208

End point title	Pharmacokinetic (PK) Parameter: Maximum Serum
-----------------	---

End point description:

The highest concentration of MOR00208 measured in serum

End point type Secondary

End point timeframe:

Estimated from first dose (samples taken on first day of dosing at pre-dose, end of infusion, after 1 hour, 4 hours, 24 hours, and pre-dose on Day 8)

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	85 ^[5]			
Units: µg/mL				
arithmetic mean (standard deviation)	263.1 (± 111.35)			

Notes:

[5] - PK parameters were calculated as data permitted for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Time to Maximum Serum Concentration Observed (Tmax) of MOR00208

End point title PK Parameter: Time to Maximum Serum Concentration Observed (Tmax) of MOR00208

End point description:

The time to highest concentration of MOR00208 measured in serum

End point type Secondary

End point timeframe:

Estimated from first dose (samples taken on first day of dosing at pre-dose, end of infusion, after 1 hour, 4 hours, 24 hours, and pre-dose on Day 8)

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	85 ^[6]			
Units: hours				
arithmetic mean (standard deviation)	5.8 (± 17.46)			

Notes:

[6] - PK parameters were calculated as data permitted for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Apparent Trough Serum Concentration Before Dosing (Clast) of MOR00208

End point title	PK Parameter: Apparent Trough Serum Concentration Before Dosing (Clast) of MOR00208
End point description:	The last quantifiable concentration from the first dose of MOR00208
End point type	Secondary
End point timeframe:	Estimated from first dose (samples taken on first day of dosing at pre-dose, end of infusion, after 1 hour, 4 hours, 24 hours, and pre-dose on Day 8)

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	85 ^[7]			
Units: µg/mL				
arithmetic mean (standard deviation)	81.0 (± 36.66)			

Notes:

[7] - PK parameters were calculated as data permitted for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Area Under the Concentration Curve From Dose Time Zero to the Time the Last Quantifiable Concentration is Observed (AUC[0-t]) of MOR00208

End point title	PK Parameter: Area Under the Concentration Curve From Dose Time Zero to the Time the Last Quantifiable Concentration is Observed (AUC[0-t]) of MOR00208
End point description:	Area under the concentration curve. The time curve from time zero (0) to the time that the last concentration above the lower limit of quantification (LLQ) is observed.
End point type	Secondary
End point timeframe:	Estimated from first dose (samples taken on first day of dosing at pre-dose, end of infusion, after 1 hour, 4 hours, 24 hours, and pre-dose on Day 8)

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	85 ^[8]			
Units: h*µg/mL				
arithmetic mean (standard deviation)	21942.5 (± 11847.35)			

Notes:

[8] - PK parameters were calculated as data permitted for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Apparent Terminal Rate Constant (λ_z) of MOR00208

End point title	PK Parameter: Apparent Terminal Rate Constant (λ_z) of MOR00208
End point description: Apparent terminal rate constant calculated from the regression analysis (slope) from the log-transformed measured concentrations on the terminal phase of the time-point concentration curve	
End point type	Secondary
End point timeframe: Estimated from final dose (samples collected on the last day of Cycle 3 [C3D28; each cycle is 28 days long], and Follow-up Visits 1 [C3D28 + 4 weeks], 2 [C3D28 + 10 weeks], and 3 [C3D28 + 16 weeks])	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	12 ^[9]			
Units: 1/h				
arithmetic mean (standard deviation)	0.00214 ($\pm$ 0.000665)			

Notes:

[9] - PK parameters were calculated as data permitted for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Apparent Terminal Half-life ($t_{1/2}$) of MOR00208

End point title	PK Parameter: Apparent Terminal Half-life ($t_{1/2}$) of MOR00208
End point description: Apparent terminal half-life calculated from $\ln(2)/\lambda_z$	
End point type	Secondary
End point timeframe: Estimated from final dose (samples collected on the last day of Cycle 3 [C3D28; each cycle is 28 days long], and Follow-up Visits 1 [C3D28 + 4 weeks], 2 [C3D28 + 10 weeks], and 3 [C3D28 + 16 weeks])	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	12 ^[10]			
Units: days				
arithmetic mean (standard deviation)	14.75111 ($\pm$ 4.680075)			

Notes:

[10] - PK parameters were calculated as permitted for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Measurements of B-cell Populations

End point title	Absolute Change From Baseline in Measurements of B-cell Populations
End point description: Actual change from baseline will be summarized descriptively by visit for the pharmacodynamic parameter: B-cell populations	
End point type	Secondary
End point timeframe: Cycle 1 Day 1 (Baseline) to Cycle 1: Days 8, 15, and 22; Cycles 2 and 3: Days 1, 15, and 28 (each cycle is 28 days); End of Study (up to 7.5 years)	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	70 ^[11]			
Units: 10 ⁶ /L				
median (confidence interval 95%)				
Cycle 1 Day 8	-13.60 (-50.250 to -1.000)			
Cycle 1 Day 15	-15.00 (-55.940 to -3.000)			
Cycle 1 Day 22	-14.00 (-57.000 to -4.500)			
Cycle 2 Day 1	-14.00 (-51.710 to -3.600)			
Cycle 2 Day 15	-24.00 (-61.000 to -12.000)			
Cycle 2 Day 28	-27.68 (-59.000 to -8.000)			
Cycle 3 Day 1	-36.00 (-117.990 to 0.000)			
Cycle 3 Day 15	-36.50 (-135.720 to 0.000)			
Cycle 3 Day 28	-46.00 (-94.000 to -8.370)			
Study Completion/Early Termination	-15.00 (-69.820 to 4.000)			

Notes:

[11] - Pharmacodynamic samples were collected at timepoints through the study where possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Measurements of B-cell Populations

End point title	Percent Change From Baseline in Measurements of B-cell Populations
End point description: Relative change from baseline will be summarized descriptively by visit for the pharmacodynamic parameter: B-cell populations	
End point type	Secondary
End point timeframe: Cycle 1 Day 1 (Baseline) to Cycle 1: Days 8, 15, and 22; Cycles 2 and 3: Days 1, 15, and 28 (each cycle is 28 days); End of Study (up to 7.5 years)	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	70 ^[12]			
Units: percentage change from baseline				
median (confidence interval 95%)				
Cycle 1 Day 8	-42.07 (-70.588 to -2.793)			
Cycle 1 Day 15	-50.00 (-79.422 to -32.353)			
Cycle 1 Day 22	-55.88 (-82.625 to -27.500)			
Cycle 2 Day 1	-55.63 (-80.000 to -27.273)			
Cycle 2 Day 15	-73.80 (-83.542 to -57.407)			
Cycle 2 Day 28	-76.47 (-86.458 to -38.095)			
Cycle 3 Day 1	-79.63 (-94.585 to -3.666)			
Cycle 3 Day 15	-72.07 (-93.953 to -33.333)			
Cycle 3 Day 28	-80.00 (-95.833 to -53.191)			
Study Completion/Early Termination	-49.31 (-85.444 to 2.941)			

Notes:

[12] - Pharmacodynamic samples were collected at timepoints through the study where possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Measurements of T-cell Populations

End point title	Absolute Change From Baseline in Measurements of T-cell Populations
End point description: Actual change from baseline will be summarized descriptively by visit for the pharmacodynamic parameter: T-cell populations	
End point type	Secondary
End point timeframe: Cycle 1 Day 1 (Baseline) to Cycle 1: Days 8, 15, and 22; Cycles 2 and 3: Days 1, 15, and 28 (each cycle is 28 days); End of Study (up to 7.5 years)	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	71 ^[13]			
Units: 10 ⁶ /L				
median (confidence interval 95%)				
Cycle 1 Day 8	41.00 (-3.460 to 89.000)			
Cycle 1 Day 15	12.00 (-67.000 to 80.000)			
Cycle 1 Day 22	-10.00 (-70.880 to 34.000)			
Cycle 2 Day 1	17.50 (-100.000 to 61.000)			
Cycle 2 Day 15	88.00 (-9.000 to 152.000)			
Cycle 2 Day 28	99.00 (-17.000 to 250.000)			
Cycle 3 Day 1	58.00 (-69.000 to 158.500)			
Cycle 3 Day 15	110.00 (-27.000 to 318.000)			
Cycle 3 Day 28	102.45 (-40.000 to 243.000)			
Study Completion/Early Termination	-57.50 (-137.000 to 144.000)			

Notes:

[13] - Pharmacodynamic samples were collected at timepoints through the study where possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Measurements of T-cell Populations

End point title	Percent Change From Baseline in Measurements of T-cell Populations
End point description: Relative change from baseline will be summarized descriptively by visit for the pharmacodynamic parameter: T-cell populations	

End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Baseline) to Cycle 1: Days 8, 15, and 22; Cycles 2 and 3: Days 1, 15, and 28 (each cycle is 28 days); End of Study (up to 7.5 years)	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	71 ^[14]			
Units: percentage change from baseline				
median (confidence interval 95%)				
Cycle 1 Day 8	7.28 (-0.394 to 16.991)			
Cycle 1 Day 15	1.75 (-9.999 to 12.312)			
Cycle 1 Day 22	-1.63 (-10.213 to 6.436)			
Cycle 2 Day 1	2.93 (-12.484 to 12.025)			
Cycle 2 Day 15	10.39 (-1.170 to 22.944)			
Cycle 2 Day 28	9.91 (-3.321 to 30.339)			
Cycle 3 Day 1	12.99 (-6.114 to 23.810)			
Cycle 3 Day 15	20.09 (-7.627 to 34.934)			
Cycle 3 Day 28	17.34 (-9.783 to 26.905)			
Study Completion/Early Termination	-8.07 (-14.994 to 26.912)			

Notes:

[14] - Pharmacodynamic samples were collected at timepoints through the study where possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Baseline in Measurements of NK Cell Populations

End point title	Absolute Change From Baseline in Measurements of NK Cell Populations
End point description:	
Actual change from baseline will be summarized descriptively by visit for the pharmacodynamic parameter: NK cell populations	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Baseline) to Cycle 1: Days 8, 15, and 22; Cycles 2 and 3: Days 1, 15, and 28 (each cycle is 28 days); End of Study (up to 7.5 years)	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	71 ^[15]			
Units: 10 ⁶ /L				
median (confidence interval 95%)				
Cycle 1 Day 8	-2.20 (-21.000 to 15.000)			
Cycle 1 Day 15	-23.00 (-43.000 to 11.000)			
Cycle 1 Day 22	-18.00 (-38.000 to 7.550)			
Cycle 2 Day 1	-16.32 (-33.000 to 9.890)			
Cycle 2 Day 15	-19.00 (-32.000 to 16.800)			
Cycle 2 Day 28	-1.00 (-18.000 to 51.000)			
Cycle 3 Day 1	-23.00 (-66.000 to -3.000)			
Cycle 3 Day 15	-33.00 (-70.000 to -2.000)			
Cycle 3 Day 28	-15.00 (-32.000 to 11.000)			
Study Completion/Early Termination	-11.00 (-35.000 to 2.000)			

Notes:

[15] - Pharmacodynamic samples were collected at timepoints through the study where possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Measurements of NK Cell Populations

End point title	Percent Change From Baseline in Measurements of NK Cell Populations
End point description: Relative change from baseline will be summarized descriptively by visit for the pharmacodynamic parameter: NK cell populations	
End point type	Secondary
End point timeframe: Cycle 1 Day 1 (Baseline) to Cycle 1: Days 8, 15, and 22; Cycles 2 and 3: Days 1, 15, and 28 (each cycle is 28 days); End of Study (up to 7.5 years)	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	71 ^[16]			
Units: percentage change from baseline				
median (confidence interval 95%)				
Cycle 1 Day 8	-1.62 (-18.261 to 11.429)			
Cycle 1 Day 15	-18.85 (-24.046 to 11.364)			
Cycle 1 Day 22	-13.38 (-29.688 to 3.027)			
Cycle 2 Day 1	-11.17 (-23.478 to 5.634)			
Cycle 2 Day 15	-8.11 (-22.467 to 20.314)			
Cycle 2 Day 28	-1.92 (-14.762 to 29.730)			
Cycle 3 Day 1	-14.08 (-26.866 to -1.115)			
Cycle 3 Day 15	-20.13 (-38.253 to -1.136)			
Cycle 3 Day 28	-6.10 (-21.697 to 17.000)			
Study Completion/Early Termination	-11.01 (-28.906 to 6.667)			

Notes:

[16] - Pharmacodynamic samples were collected at timepoints through the study where possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of AEs Stratified by FcγRIIa Polymorphism

End point title	Evaluation of AEs Stratified by FcγRIIa Polymorphism
End point description:	
Incidence of AEs as stratified by FcγRIIa polymorphism subgroups	
End point type	Secondary
End point timeframe:	
From first dose until 30 days after last dose of MOR00208, up to 8.5 years	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: adverse events				
Genotype HH	210			
Genotype HR	188			
Genotype RR	61			

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of AEs Stratified by FcγRIIIa Polymorphism

End point title	Evaluation of AEs Stratified by FcγRIIIa Polymorphism
-----------------	---

End point description:

Incidence of AEs as stratified by FcγRIIIa polymorphism subgroups

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

End point timeframe:

From first dose until 30 days after last dose of MOR00208, up to 8.5 years

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	74			
Units: adverse events				
Genotype FF	110			
Genotype FV	149			
Genotype VV	200			

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of ORR Stratified by FcγRIIa Polymorphism

End point title	Evaluation of ORR Stratified by FcγRIIa Polymorphism
-----------------	--

End point description:

The analysis of the primary endpoint (ORR) will additionally be stratified by FcγRIIa polymorphism subgroups

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

End point timeframe:

From first dose until Follow-up Visit 12, up to 4.5 years

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: patients				
Genotype HH	6			
Genotype HR	8			
Genotype RR	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of ORR Stratified by FcγRIIIa Polymorphism

End point title	Evaluation of ORR Stratified by FcγRIIIa Polymorphism
End point description: The analysis of the primary endpoint (ORR) will additionally be stratified by FcγRIIIa polymorphism subgroups	
End point type	Secondary
End point timeframe: From first dose until Follow-up Visit 12, up to 4.5 years	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: patients				
Genotype FF	10			
Genotype FV	5			
Genotype VV	2			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Area Under the Concentration Curve From Dose Time Zero to Infinity (AUC[0-inf]) of MOR00208

End point title	PK Parameter: Area Under the Concentration Curve From Dose Time Zero to Infinity (AUC[0-inf]) of MOR00208
End point description: Area under the concentration curve. The time curve from time zero (0) to infinity (inf), where infinity is computed from $AUC_{0-t} + [C_t/\lambda_Z]$. C_t is calculated from the concentration at the last sampling time at which the sample is above LLQ.	
End point type	Secondary
End point timeframe: Estimated from final dose (samples collected on the last day of Cycle 3 [C3D28; each cycle is 28 days long], and Follow-up Visits 1 [C3D28 + 4 weeks], 2 [C3D28 + 10 weeks], and 3 [C3D28 + 16 weeks])	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	91 ^[17]			
Units: h*µg/mL				
arithmetic mean (standard deviation)	0 (± 0)			

Notes:

[17] - The parameter could not be accurately estimated for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Total Body Clearance (CL) of MOR00208

End point title	PK Parameter: Total Body Clearance (CL) of MOR00208
End point description:	
Total body clearance calculated for single or multiple doses: dose(s)/AUC(0-inf)	
End point type	Secondary
End point timeframe:	
Estimated from final dose (samples collected on the last day of Cycle 3 [C3D28; each cycle is 28 days long], and Follow-up Visits 1 [C3D28 + 4 weeks], 2 [C3D28 + 10 weeks], and 3 [C3D28 + 16 weeks])	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	91 ^[18]			
Units: L/h				
arithmetic mean (standard deviation)	0 (± 0)			

Notes:

[18] - The parameter could not be accurately estimated for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Apparent Volume of Distribution (V_z) of MOR00208

End point title	PK Parameter: Apparent Volume of Distribution (V _z) of MOR00208
End point description:	
Apparent volume of distribution during the terminal phase, calculated from dose/(AUC(0-inf)*λ _z)	
End point type	Secondary
End point timeframe:	
Estimated from final dose (samples collected on the last day of Cycle 3 [C3D28; each cycle is 28 days long], and Follow-up Visits 1 [C3D28 + 4 weeks], 2 [C3D28 + 10 weeks], and 3 [C3D28 + 16 weeks])	

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	91 ^[19]			
Units: L				
arithmetic mean (standard deviation)	0 (± 0)			

Notes:

[19] - The parameter could not be accurately estimated for the PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of AEs Stratified by Baseline CD19 Expression on Malignant Lymphoma Cells

End point title	Evaluation of AEs Stratified by Baseline CD19 Expression on Malignant Lymphoma Cells
End point description:	Incidence of AEs as stratified by presence of CD19 on malignant lymphoma cells detected by tumor biopsy/aspirate during Screening
End point type	Secondary
End point timeframe:	From first dose until 30 days after last dose of MOR00208, up to 8.5 years

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[20]			
Units: adverse events				

Notes:

[20] - CD19 expression could not be measured in sufficient cases for such an analysis to be meaningful.

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of ORR Stratified by Baseline CD19 Expression on Malignant Lymphoma Cells

End point title	Evaluation of ORR Stratified by Baseline CD19 Expression on Malignant Lymphoma Cells
End point description:	The analysis of the primary endpoint (ORR) will additionally be stratified by presence of CD19 on malignant lymphoma cells detected by tumor biopsy/aspirate during Screening
End point type	Secondary
End point timeframe:	From first dose until Follow-up Visit 12, up to 4.5 years

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[21]			
Units: patients				

Notes:

[21] - CD19 expression could not be measured in sufficient cases for such an analysis to be meaningful.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from informed consent until 30 days after last dose of MOR00208, up to 8.5 years

Adverse event reporting additional description:

AEs were detected when volunteered by the patient during or between study visits or through physical examination, laboratory tests, or other assessments. All SAEs are reported, including non-treatment-emergent events. For non-serious AEs, only treatment-emergent events are reported.

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

Dictionary used

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

Dictionary version	24.0
--------------------	------

Reporting groups

Reporting group title	MOR00208
-----------------------	----------

Reporting group description:

All patients who received at least one dose of study drug.

Serious adverse events	MOR00208		
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 92 (32.61%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	9		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bone cancer			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			

subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	11 / 92 (11.96%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 8		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 92 (2.17%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			

subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 92 (3.26%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Genital herpes zoster			

subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	2 / 92 (2.17%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infected bite			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumococcal infection			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MOR00208		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 92 (83.70%)		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	12 / 92 (13.04%)		
occurrences (all)	15		
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	9 / 92 (9.78%) 11		
Headache subjects affected / exposed occurrences (all)	10 / 92 (10.87%) 15		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	6 / 92 (6.52%) 9		
Neutropenia subjects affected / exposed occurrences (all)	9 / 92 (9.78%) 12		
Thrombocytopenia subjects affected / exposed occurrences (all)	5 / 92 (5.43%) 14		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	7 / 92 (7.61%) 9		
Oedema peripheral subjects affected / exposed occurrences (all)	8 / 92 (8.70%) 9		
Fatigue subjects affected / exposed occurrences (all)	8 / 92 (8.70%) 12		
Pyrexia subjects affected / exposed occurrences (all)	5 / 92 (5.43%) 8		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	8 / 92 (8.70%) 9		
Constipation subjects affected / exposed occurrences (all)	6 / 92 (6.52%) 7		

Nausea subjects affected / exposed occurrences (all)	9 / 92 (9.78%) 11		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	7 / 92 (7.61%) 9 8 / 92 (8.70%) 14		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	7 / 92 (7.61%) 8		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	7 / 92 (7.61%) 7		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all)	11 / 92 (11.96%) 14 6 / 92 (6.52%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2013	1. A clinical deficiency/information request from FDA dated 05 October 2012. 2. A clinical deficiency/information request from FDA dated 11 October 2012. 3. Minor inconsistencies identified and organizational changes made since release of the original protocol, none of which constitute a change in the conduct or scientific value of the study.
02 October 2013	1. Organizational issues that came up during the initiation of the first study sites. 2. Minor inconsistencies identified and organizational changes made since the release of the original protocol, none of which constituted a change in the conduct or scientific value of the study.
15 April 2014	1. New recommendations for the screening of hepatitis B for anti-CD20 antibodies were published. 2. Minor inconsistencies identified and organizational changes were made since the release of the previous amendment, none of which constitute a change in the conduct or scientific value of the study.
19 September 2017	1. Change of address of sponsor and CRO. 2. Addition of optional prolongation of maintenance treatment for patients beyond Follow-up Visit 12 until progression. 3. Change of sponsor signatories and change of key personnel at sponsor and CRO. 4. Change of data collection as a result of this amendment. 5. Minor editorial changes for clarification of content and removal of inconsistencies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported