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	

Results information

Result version number	v1
This version publication date	05 January 2019
First version publication date	05 January 2019

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	Sascha Tillmanns, Morphosys AG, 0049 89 89927 26520, Sascha.tillmanns@morphosys.com
Scientific contact	Sascha Tillmanns, Morphosys AG, 0049 89 89927 26520, Sascha.tillmanns@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	Interim
Date of interim/final analysis	31 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2015
Global end of trial reached?	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 Harmonization (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 will include 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	Belgium: 2
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	United States: 20
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 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	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:

1. Pts were male or female ≥ 18 years of age. 2. Pts with a histologically confirmed diagnosis of DLBCL, FL, MCL or other indolent NHL (e.g., MZL/MALT). 3. Progression after at least 1 prior rituximab-containing regimen. 4. At least one site of measurable disease on MRI or CT.

Period 1

Period 1 title	MOR00208 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	MOR00208

Arm description:

MOR00208 12 mg/kg. The study population consisted of adult patients with relapsed or refractory B-cell NHL who had received at least 1 completed cycle of combination therapy with rituximab + chemotherapy or at least 4 weekly administrations of rituximab as monotherapy.

Arm type	Experimental
Investigational medicinal product name	MOR00208
Investigational medicinal product code	MOR00208
Other name	
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.

Number of subjects in period 1	MOR00208
Started	92
Completed	72
Not completed	20
Adverse event, serious fatal	4
Physician decision	2
new cancer treatment	1
Adverse event, non-fatal	3
Progressive disease	9
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	MOR00208
Reporting group description:	
MOR00208 12 mg/kg. The study population consisted of adult patients with relapsed or refractory B-cell NHL who had received at least 1 completed cycle of combination therapy with rituximab + chemotherapy or at least 4 weekly administrations of rituximab as monotherapy.	

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	65.6		
standard deviation	± 12.23	-	
Gender categorical			
Units: Subjects			
Female	36	36	
Male	56	56	
Weight			
Units: kg			
arithmetic mean	77.1		
standard deviation	± 17.01	-	
BMI			
Units: kg/m2			
arithmetic mean	26.86		
standard deviation	± 5.13	-	
Height			
Height			
Units: cm			
arithmetic mean	169.3		
standard deviation	± 11.95	-	

End points

End points reporting groups

Reporting group title	MOR00208

Reporting group description:

MOR00208 12 mg/kg. The study population consisted of adult patients with relapsed or refractory B-cell NHL who had received at least 1 completed cycle of combination therapy with rituximab + chemotherapy or at least 4 weekly administrations of rituximab as monotherapy.

Primary: Overall response rate

End point title	Overall response rate[1]

End point description:

Overall response rate (CR+PR; complete and partial remission), assessed as per the 2007 International Working Group (IWG) response criteria

End point type	Primary

End point timeframe:

Total study period

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 clinical trial was analysed descriptively.

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: number	21			

Statistical analyses

No statistical analyses for this end point

Secondary: Stable disease

End point title	Stable disease

End point description:

Number of patients on stable disase

End point type	Secondary

End point timeframe:

Total study period

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: numbers	32			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression

End point title	Time to progression

End point description:

Assessed by the investigator rate of progression of the total population (all subsets) until date of first tumor progression.

End point type	Secondary

End point timeframe:

Total study period

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: Months				
median (confidence interval 95%)	6.0 (3.4 to 12.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

Progression free survival was defined as the time from cycle 1 day 1 until date of first tumor progression or date of death from any cause.

End point type	Secondary

End point timeframe:

Total study period

End point values	MOR00208			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: Months				
median (confidence interval 95%)	5.4 (3.2 to 9.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

To ensure patient safety, every SAE/AE, regardless of suspected causality, occurring after the patient had provided informed consent and untill 30 days after the patient had stopped study participation was to be recorded.

Adverse event reporting additional description:

Adverse events were coded according to MedDRA (version 14) system organ class (SOC) and preferred term. Incidence of all adverse events was summarized by SOC, preferred term, relationship to treatment, severity and seriousness. Adverse events were summarized overall and by each NHL subtype.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	MOR00208

Reporting group description:

MOR00208 patients with at least one infusion of drug

Serious adverse events	MOR00208		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 92 (30.43%)		
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		
Injury, poisoning and procedural complications			
Fracture			
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	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
dIsease progression			
subjects affected / exposed	8 / 92 (8.70%)		
occurrences causally related to treatment / all	8 / 8		
deaths causally related to treatment / all	8 / 8		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 92 (2.17%)		
occurrences causally related to treatment / all	2 / 2		
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		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Colitits			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal hemorrhage			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
respiratory failure1			

subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
pneumonia			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Genital Herpes			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
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	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infected bites			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 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	1 / 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	76 / 92 (82.61%)		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	11 / 92 (11.96%)		
occurrences (all)	14		
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 92 (9.78%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	10 / 92 (10.87%)		
occurrences (all)	15		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	8 / 92 (8.70%)		
occurrences (all)	11		
Lymphadenopathy			

subjects affected / exposed	5 / 92 (5.43%)		
occurrences (all)	9		
Thormbocytopenia			
subjects affected / exposed	5 / 92 (5.43%)		
occurrences (all)	14		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 92 (7.61%)		
occurrences (all)	9		
Chillis			
subjects affected / exposed	5 / 92 (5.43%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	8 / 92 (8.70%)		
occurrences (all)	11		
Oedema peripheral			
subjects affected / exposed	9 / 92 (9.78%)		
occurrences (all)	11		
Pyrexia			
subjects affected / exposed	5 / 92 (5.43%)		
occurrences (all)	8		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 92 (6.52%)		
occurrences (all)	7		
Diarrhoea			
subjects affected / exposed	8 / 92 (8.70%)		
occurrences (all)	9		
Nausea			
subjects affected / exposed	9 / 92 (9.78%)		
occurrences (all)	11		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 92 (8.70%)		
occurrences (all)	11		
Dyspnoea			

subjects affected / exposed occurrences (all)	8 / 92 (8.70%) 10		
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)	 10 / 92 (10.87%) 12 5 / 92 (5.43%) 6		
Metabolism and nutrition disorders Hypokalemia subjects affected / exposed occurrences (all)	 5 / 92 (5.43%) 12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2013	Clinical deficiency/information request from FDA dated 05 October 2012, a clinical deficiency/information request from FDA dated 11 October 2012 and 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 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.
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 and 5. Minor editorial changes for clarification of contant and removal of inconsistencies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported