Clinical trial results:
A Phase II, Single-Arm, Open-Label, Multicentre Study to Evaluate the Safety and Efficacy of Lenalidomide Combined with MOR00208 in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (R-R DLBCL)

Summary

EudraCT number	2014-004688-19
Trial protocol	IT CZ HU DE ES FR BE
Global end of trial date	14 November 2022

Results information

Result version number	v1 (current)
This version publication date	25 October 2023
First version publication date	25 October 2023

Trial information

Trial identification

Sponsor protocol code	MOR208C203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02399085
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MorphoSys AG
Sponsor organisation address	Semmelweisstr. 7, Planegg, Germany, 82152
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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	14 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective
1. To determine the activity of a combination of LEN with MOR00208 in terms of objective response rate (ORR)
(ORR = complete response [CR] + partial response [PR]) in adult subjects with R-R DLBCL
Secondary Objectives:
1. To determine the disease control rate (DCR = CR + PR + stable disease [SD])
2. To determine the duration of response (DoR)
3. To determine the activity of a combination of LEN with MOR00208 in terms of progression-free survival (PFS)
4. To determine the overall survival (OS)
5. To determine time to progression (TTP)
6. To determine the time to next treatment (TTNT)
7. To determine the safety of LEN combined with MOR00208 assessed according to the frequency and severity of adverse events (AEs)
8. To assess the potential immunogenicity of MOR00208
9. To assess the pharmacokinetics (PK) of MOR00208
10. To evaluate ORR, DCR, DoR, PFS, OS, TTP and TTNT in subjects treated with a combination of LEN plus MOR00208 in cohorts

Protection of trial subjects:

This clinical study was designed and conducted and reported in accordance with the protocol, with ICH E6 GCP guidelines, with applicable local regulations, and with the ethical principles laid down in the Declaration of Helsinki, including, but not limited to:
1. IRB/IEC review and favorable opinion/approval of the study protocol and any subsequent amendments
2. Subjects informed consent
3. Investigator reporting requirements
4. Sponsor provided full details of the above procedures, either verbally, in writing, or both.
5. In cohorts with a “low risk”, “low intermediate”, “high-intermediate” and “high” International Prognostic Index (IPI). To compare each subject's time to progression (TTP) on LEN plus MOR00208 with the TTP of their most recent prior therapy. To correlate efficacy parameters with certain biomarkers (e.g., baseline tumour CD19 expression level, peripheral NK cell count, constitutional FcγRIIIa and FcγRIIapolymorphism status).
No substantial changes to the final approved protocol was initiated without the IRB’s/IEC’s prior written approval or favorable opinion and approval by the regulatory bodies/local health authorities of a written amendment, except when necessary to eliminate immediate hazards to the subjects or when the change involves only logistics or administration.
The ICF must be signed, with name and date noted by the subjects, before the subject was exposed to any study-related procedure, including screening tests for eligibility.
Study monitoring was performed in accordance with ICH E6 GCP guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Spain: 15
Worldwide total number of subjects	81
EEA total number of subjects	70

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)	23
From 65 to 84 years	57
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The subjects were enrolled into this study at sites in Hungary, Belgium, Czechia, France, Poland, Italy, Germany, Spain, United kingdom, and the United States.

Pre-assignment

Screening details:

For female child bearing subjects the first, a serum pregnancy test was performed at screening within 10-14 days prior to the start of study drug and the second, a medically supervised urine pregnancy test was done within 24 hours prior to the start of study drug. The results of both tests had to be negative in order to receive Cycle 1 Day 1

Period 1

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

Blinding implementation details:

This was an open-label study; thus, no blinding occurred in the study.

Arms

Arm title	Tafasitamab (MOR00208) + Lenalidomide

Arm description:

MOR00208 and Lenalidomide:
Tafasitamab (MOR00208) + Lenalidomide (LEN) were administered.

Arm type	Experimental
Investigational medicinal product name	Tafasitamab
Investigational medicinal product code	MOR00208
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

MOR00208:
MOR00208 was administered via IV infusion at a dose of 12 mg/kg. For the first three cycles (Cycles 1 to 3) of the study each cycle consisted of a
MOR00208 infusion on Day 1, Day 8, Day 15 and Day 22 of the cycle. Additionally, a loading dose was administered on Day 4 of Cycle 1. Thereafter MOR00208 was administered on a bi-weekly (every 14 days) basis with infusions on Day 1 and Day 15 of each 28-day cycle.

Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	LEN
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LEN:
Subjects self-administered a starting dose of 25 mg oral LEN daily on Days 1-21 of each cycle, for up to 12 cycles in total. LEN dose could be
modified in a de-escalating fashion or discontinued based upon clinical and laboratory findings.

Number of subjects in period 1	Tafasitamab (MOR00208) + Lenalidomide
Started	81
Received MOR00208 and Lenalidomide	80
Received Tafa Only	1 [1]
Completed	8
Not completed	73
Consent withdrawn by subject	8
Physician decision	5
Adverse event, non-fatal	16
Death	2
Progressive disease	42

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: 80 subjects received Tafasitamab (MOR00208) + Lenalidomide (Len) and 1 subject received MOR00208 only.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment (MOR00208 + Lenalidomide)

Reporting group description: -

Reporting group values	Treatment (MOR00208 + Lenalidomide)	Total	
Number of subjects	81	81	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	23	23	
From 65-84 years	57	57	
85 years and over	1	1	
Age continuous			
Units: years			
arithmetic mean	69.3		
standard deviation	± 9.53	-	
Gender categorical			
Units: Subjects			
Female	44	44	
Male	37	37	

End points

End points reporting groups

Reporting group title	Tafasitamab (MOR00208) + Lenalidomide

Reporting group description:

MOR00208 and Lenalidomide:
Tafasitamab (MOR00208) + Lenalidomide (LEN) were administered.

Primary: Number of Participants With Best Objective Response Rate (ORR)

End point title	Number of Participants With Best Objective Response Rate (ORR)[1]

End point description:

ORR = complete response [CR] + partial response [PR]; Independent Radiology/Clinical Review Committee (IRC) Evaluation.
ORR after MOR00208 and Lenalidomide combination therapy assessed by the IRC evaluation.
ORR was defined as the number of subjects of the total number of participants treated with MOR00208 + LEN with CR or PR as best response achieved at any time during the study.

End point type	Primary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled

Notes:

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

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Number of Subjects				
Approx 4.5 years after first participant enrolled	46			
Approx 6.5 years after first participant enrolled	46			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) by IRC Evaluation

End point title	Duration of Response (DoR) by IRC Evaluation

End point description:

DoR [months] = (date of assessment of tumor progression or death – date of assessment of first documented response of (CR or PR) + 1)/30.4375.
Inclusive of subjects with available data.
Here 9999.99 has been used if the Upper limit and median not reached. The upper limit and median not reached due to insufficient number of events at later stages of follow-up.

End point type	Secondary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled.

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: Months				
median (confidence interval 95%)				
Approx 4.5 years after first participant enrolled	43.9 (26.1 to 9999.99)			
Approx 6.5 years after first participant enrolled	9999.99 (33.8 to 9999.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: DoR by Investigator (INV) Evaluation

End point title	DoR by Investigator (INV) Evaluation

End point description:

DoR [months] = (date of assessment of tumour progression or death – date of assessment of first documented response of (CR or PR) + 1)/30.4375
Inclusive of subjects with available data.
Here 9999.99 has been used if the Upper limit not reached. The upper limit not reached due to insufficient number of events at later stages of follow-up.

End point type	Secondary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled.

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Months				
median (confidence interval 95%)				
Approx 4.5 years after first participant enrolled	43.9 (13.9 to 9999.99)			
Approx 6.5 years after first participant enrolled	43.4 (14.1 to 9999.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) by IRC Evaluation

End point title	Progression-free Survival (PFS) by IRC Evaluation

End point description:

PFS time was defined as the time (in months) from the date of the first administration of any study drug to the date of tumor progression or death from any cause. Inclusive of subjects with available data.

End point type	Secondary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Months				
median (confidence interval 95%)				
Approx 4.5 years after first participant enrolled	11.6 (6.3 to 45.7)			
Approx 6.5 years after first participant enrolled	11.6 (5.7 to 45.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS by INV Evaluation

End point title	PFS by INV Evaluation

End point description:

PFS time was defined as the time (in months) from the date of the first administration of any study drug to the date of tumor progression or death from any cause. Inclusive of subjects with available data.

End point type	Secondary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: Months				
median (confidence interval 95%)				

4.5 years: n = 46 6.5 years: n = 49	9.1 (5.5 to 28.0) 9.1 (5.5 to 45.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from the date of the first administration of any study drug until death from any cause (documented by the date of death).
Inclusive of subjects with available data.
Here 9999.99 has been used if the Upper limit not reached. The upper limit not reached due to insufficient number of events at later stages of follow-up.

End point type	Secondary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Months				
median (confidence interval 95%)				
4.5 years: n = 41 6.5 years: n = 44	33.5 (18.3 to 9999.99) 33.5 (18.3 to 9999.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) by IRC Evaluation

End point title	Disease Control Rate (DCR) by IRC Evaluation

End point description:

DCR = CR + PR + SD (Stable disease); IRC Evaluation DCR was defined as the number of subjects having CR, PR or SD based on the best objective response achieved at any time during the study.

End point type	Secondary

End point timeframe:

Approximately 2.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Number of Subjects	59			

Statistical analyses

No statistical analyses for this end point

Secondary: DCR by INV Evaluation

End point title	DCR by INV Evaluation

End point description:

DCR = CR + PR + SD (Stable disease); IRC Evaluation DCR was defined as the number of subjects having CR, PR or SD based on the best objective response achieved at any time during the study.

End point type	Secondary

End point timeframe:

Approximately 2.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Number of Subjects	60			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP) by IRC Evaluation

End point title	Time to Progression (TTP) by IRC Evaluation

End point description:

TTP is defined as the time from the first administration of any study drug until documented DLBCL progression or death as a result of lymphoma.
Inclusive of subjects with available data.
Here 9999.99 has been used if the Upper limit not reached. The upper limit not reached due to insufficient number of events at later stages of follow-up.

End point type	Secondary

End point timeframe:

Approximately 2.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Months				
median (confidence interval 95%)	16.2 (7.4 to 9999.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: TTP by INV Evaluation

End point title	TTP by INV Evaluation

End point description:

TTP is defined as the time from the first administration of any study drug until documented DLBCL progression or death as a result of lymphoma.
Inclusive of subjects with available data.
Here 9999.99 has been used if the upper limit not reached. The upper limit not reached due to insufficient number of events at later stages of follow-up.

End point type	Secondary

End point timeframe:

Approximately 2.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Months				
median (confidence interval 95%)	14.1 (6.3 to 9999.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Treatment (TTNT)

End point title	Time to Next Treatment (TTNT)

End point description:

Kaplan-Meier analysis of TTNT in FAS population. TTNT is defined as the time from the first administration of any study drug to the institution of next anti-neoplastic therapy (for any reason including disease progression, treatment toxicity and subject preference) or death of any cause, whatever comes first.
Inclusive of subjects with available data.

End point type	Secondary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Months				
median (confidence interval 95%)				
4.5 years: n = 51 6.5 years: n = 55	12.1 (7.3 to 24.7) 12.5 (7.3 to 28.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival (EFS)

End point title	Event-free Survival (EFS)

End point description:

EFS is defined as the time (in months) from the date of the first administration of any study drug to the date of tumour progression, first initiation of a new non-study anti-neoplastic therapy or death from any cause whichever comes first.
Inclusive of subjects with available data.

End point type	Secondary

End point timeframe:

Approximately 4.5 years after first subject enrolled; Approximately 6.5 years after first subject enrolled

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Months				
median (confidence interval 95%)				
4.5 years: n = 53	8.7 (5.3 to 21.0)			

6.5 years: n = 55	9.1 (5.3 to 23.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Drug Levels of MOR00208

End point title	Serum Drug Levels of MOR00208

End point description:

The pharmacokinetics (PK) profile of MOR00208 was investigated by quantifying serum drug levels at baseline and after repeated intravenous (IV) administrations for up to 24 treatment cycles using sparse sampling.
MOR00208 PK sample was taken pre-dose and 1 hour ± 10 min after the end of MOR00208 infusion for Cycle 1 to Cycle 23. MOR00208 PK sample (pre-dose only) were taken in odd numbered additional treatment cycles only (e.g.,treatment Cycles 13, 15,17, 19, 21, 23).

End point type	Secondary

End point timeframe:

Cycle 1 Days 1, 4, 15 predose and 1 hr post-dose; Cycle 2 Days 1, 15 predose and 1 hr post-dose; Cycle 3 Days 1, 15 predose and 1 hr post-dose; Cycles 4, 5, 6, 7, 9, 11,13, 15, 17, 19, 21, 23 Day 1 predose; End of Treatment.

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (pre dose): n=79	6.7 (± 53.09)			
Cycle 1 Day 1 (1 hour post dose): n=71	249075.9 (± 53724.93)			
Cycle 1 Day 4 (pre dose): n=73	126306.8 (± 39105.37)			
Cycle 1 Day 4 (1 hour post dose): n=65	363626.2 (± 82971.54)			
Cycle 1 Day 15 (pre dose): n=75	157722.3 (± 50655.86)			
Cycle 1 Day 15 (1 hour post dose): n=70	396262.1 (± 97215.09)			
Cycle 2 Day 1 (pre dose): n=71	181870.8 (± 72582.62)			
Cycle 2 Day 1 (1 hour post dose): n=62	439788.2 (± 126930.55)			
Cycle 2 Day 15 (pre dose): n=63	217846.9 (± 77799.93)			
Cycle 2 Day 15 (1 hour post dose): n=59	442940.2 (± 85475.90)			
Cycle 3 Day 1 (pre dose): n=61	208520.6 (± 68866.46)			

Cycle 3 Day 1 (1 hour post dose): n=53	466135.8 (± 112647.31)			
Cycle 3 Day 15 (pre dose): n=51	223909.4 (± 85170.91)			
Cycle 3 Day 15 (1 hour post dose): n=44	455635.0 (± 104198.64)			
Cycle 4 Day 1 (pre dose): n=52	216328.4 (± 94553.25)			
Cycle 5 Day 1 (pre dose): n=51	142134.4 (± 72691.16)			
Cycle 6 Day 1 (pre dose): n=49	115132.3 (± 55774.77)			
Cycle 7 Day 1 (pre dose): n=49	114661.5 (± 73328.15)			
Cycle 9 Day 1 (pre dose): n=40	108640.4 (± 52282.72)			
Cycle 11 Day 1 (pre dose): n=34	126472.0 (± 64872.47)			
Cycle 13 Day 1 (pre dose): n=31	100853.5 (± 61229.42)			
Cycle 15 Day 1 (pre dose): n=30	159676.5 (± 61199.32)			
Cycle 17 Day 1 (pre dose): n=25	175855.1 (± 64592.17)			
Cycle 19 Day 1 (pre dose): n=21	197045.0 (± 69962.05)			
Cycle 21 Day 1 (pre dose): n=19	197228.0 (± 53222.03)			
Cycle 23 Day 1 (pre dose): n=15	224253.3 (± 64686.85)			
End of Treatment: n=39	141240.7 (± 114804.40)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Developed Anti-MOR00208 Antibodies

End point title	Number of Subjects Who Developed Anti-MOR00208 Antibodies

End point description:

The Anti-MOR00208 Antibodies were investigated by quantifying serum drug levels at baseline and after repeated intravenous (IV) administrations for up to 24 treatment cycles using sparse sampling. Anti-MOR00208 antibody sample (pre-dose only) were taken in odd numbered additional treatment cycles only (e.g., treatment Cycles 13, 15,17, 19, 21,23).

End point type	Secondary

End point timeframe:

Baseline, Up to a maximum of 23 cycles

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Number of Subjects				
Yes (Treatment-emergent ADAs)	0			
No (Negative baseline and post baseline results)	72			
Not evaluable (Positive baseline results)	2			
Missing (No post baseline results available)	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects That Experienced Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects That Experienced Treatment-emergent Adverse Events (TEAEs)

End point description:

TEAEs are defined as any adverse event reported in the following time interval (including the lower and upper limits): date of first administration of study treatment; date of last administration of study treatment + 30 days, or if they are considered to be related to the study drug.

End point type	Secondary

End point timeframe:

Approximately 6.5 years after first subject enrolled.

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Number of Subjects	81			

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of Treatment-emergent Adverse Events

End point title	Severity of Treatment-emergent Adverse Events

End point description:

Number of subjects with severity of treatment-emergent adverse events during MOR00208 and LEN combination therapy.

End point type	Secondary

End point timeframe:

Approximately 6.5 years after first subject enrolled.

End point values	Tafasitamab (MOR00208) + Lenalidomide			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: Number of Subjects				
Severe	43			
Moderate	31			
Mild	6			
Missing	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first day of study drug administration through 30 days after last dose, up to maximum duration of 6.5 years approximately after first subject enrolled.

Adverse event reporting additional description:

All adverse events (except non-serious adverse events for screening failures) that occurred after the provision of informed consent and up to 30 days after last study drug administration was recorded in the eCRF and in the subject's medical records, whether or not they were considered by the investigator to be related to the study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Treatment (MOR00208 + Lenalidomide)

Reporting group description:

MOR00208 was administered via intravenous Infusion, weekly (Cycle 1-3) of the study each cycle consisted of a MOR00208 infusion on Day 1, Day 8, Day 15 and Day 22 of the cycle. Additionally, a loading dose was administered on Day 4 of Cycle 1. Thereafter MOR00208 was administered on a bi-weekly (every 14 days) basis with infusions on Day 1 and Day 15 of each 28-day cycle, until disease progression or unacceptable toxicity or discontinuation due to any other reason.
Lenalidomide (Revlimid®), PO, daily, on Days 1-21 of each cycle, for up to 12 cycles in total. LEN dose could be modified in a de-escalating fashion or discontinued based upon clinical and laboratory findings. Treatment with LEN was stopped in case of disease progression, or unacceptable toxicity, or discontinuation for any other reason.
On days when both study drugs were given together, LEN was administered prior to tafasitamab.

Serious adverse events	Treatment (MOR00208 + Lenalidomide)		
Total subjects affected by serious adverse events			
subjects affected / exposed	47 / 81 (58.02%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Bowen's disease			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Breast cancer				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myelodysplastic syndrome				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myeloproliferative neoplasm				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	2 / 81 (2.47%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Tumour flare				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematoma				

subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fatigue				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	2 / 81 (2.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	3 / 81 (3.70%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				

subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound complication			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cervicobrachial syndrome			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cognitive disorder			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Facial paralysis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient global amnesia			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Febrile neutropenia			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			

subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bronchitis				
subjects affected / exposed	2 / 81 (2.47%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	3 / 81 (3.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Enterobacter bacteraemia				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				

subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis rotavirus				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral discitis				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella sepsis				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	2 / 81 (2.47%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Parainfluenzae virus infection				

subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	7 / 81 (8.64%)			
occurrences causally related to treatment / all	3 / 7			
deaths causally related to treatment / all	0 / 0			
Progressive multifocal leukoencephalopathy				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Soft tissue infection				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcal sepsis				
subjects affected / exposed	1 / 81 (1.23%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella zoster virus infection			
subjects affected / exposed	1 / 81 (1.23%)		
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	Treatment (MOR00208 + Lenalidomide)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 81 (92.59%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	10		
Hypotension			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	6		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	21 / 81 (25.93%)		
occurrences (all)	39		
Fatigue			
subjects affected / exposed	13 / 81 (16.05%)		
occurrences (all)	24		
Mucosal inflammation			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	9		

Oedema peripheral subjects affected / exposed occurrences (all)	20 / 81 (24.69%) 35		
Pyrexia subjects affected / exposed occurrences (all)	18 / 81 (22.22%) 39		
Immune system disorders Hypogammaglobulinaemia subjects affected / exposed occurrences (all)	5 / 81 (6.17%) 5		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	24 / 81 (29.63%) 36		
Dyspnoea subjects affected / exposed occurrences (all)	10 / 81 (12.35%) 16		
Oropharyngeal pain subjects affected / exposed occurrences (all)	6 / 81 (7.41%) 6		
Productive cough subjects affected / exposed occurrences (all)	5 / 81 (6.17%) 5		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	6 / 81 (7.41%) 10		
Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	5 / 81 (6.17%) 9		
Blood creatinine increased subjects affected / exposed occurrences (all)	7 / 81 (8.64%) 17		
C-reactive protein increased			

subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	12		
Gamma-glutamyltransferase increased			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	9		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	19		
Paraesthesia			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	7		
Sciatica			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	30 / 81 (37.04%)		
occurrences (all)	74		
Febrile neutropenia			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	6		
Leukopenia			
subjects affected / exposed	10 / 81 (12.35%)		
occurrences (all)	44		
Lymphopenia			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	10		
Neutropenia			
subjects affected / exposed	40 / 81 (49.38%)		
occurrences (all)	215		
Thrombocytopenia			

subjects affected / exposed occurrences (all)	23 / 81 (28.40%) 71		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 8 / 81 (9.88%) 9 6 / 81 (7.41%) 8 15 / 81 (18.52%) 21 30 / 81 (37.04%) 63 12 / 81 (14.81%) 21 12 / 81 (14.81%) 15		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all)	 8 / 81 (9.88%) 9 8 / 81 (9.88%) 10 5 / 81 (6.17%) 5		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	 5 / 81 (6.17%) 5		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	11		
Back pain			
subjects affected / exposed	16 / 81 (19.75%)		
occurrences (all)	19		
Muscle spasms			
subjects affected / exposed	12 / 81 (14.81%)		
occurrences (all)	16		
Pain in extremity			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	913		
Infections and infestations			
Bronchitis			
subjects affected / exposed	12 / 81 (14.81%)		
occurrences (all)	19		
Gastroenteritis			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	9		
Nasopharyngitis			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	11		
Respiratory tract infection			
subjects affected / exposed	9 / 81 (11.11%)		
occurrences (all)	17		
Rhinitis			
subjects affected / exposed	7 / 81 (8.64%)		
occurrences (all)	7		
Sinusitis			
subjects affected / exposed	6 / 81 (7.41%)		
occurrences (all)	7		
Upper respiratory tract infection			
subjects affected / exposed	8 / 81 (9.88%)		
occurrences (all)	9		
Urinary tract infection			

subjects affected / exposed occurrences (all)	10 / 81 (12.35%) 15		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all)	 18 / 81 (22.22%) 20 5 / 81 (6.17%) 18 5 / 81 (6.17%) 16 15 / 81 (18.52%) 28 8 / 81 (9.88%) 26		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2015	Protocol Amendment 1 Version 4: Study design was updated. Due to the request of the VHP Grounds for non-acceptance (GNA) dated 19 May 2015 clarification on the constitution of the safety review panel was added. Dosing schedule was changed to bi-weekly MOR00208 administration from Cycle 4. Subject inclusion /exclusion criteria were updated . Section 6 was updated due to a sponsor decision that MOR00208 was to be provided centrally only, LEN could be obtained from commercial sources (e.g., reimbursement or centrally) and other medications (e.g., pre-medication agents) were provided by participating site. Clarification on patient compliance was added. (Safety Assessments was deleted as the section was redundant. The collection of ECG RR intervals was added in the Section 7.2.5 because ECG RR intervals were needed for QTc calculations. Clarifications were made about the dipstick urine pregnancy test; sensitivity of the test was added. Re-wording and clarification was added concerning the control of blood glucose for obtaining assessable PET scan and conditions for PET/CT to replace CT while measuring the tumour. The collection of ECG QT intervals was added in Section 10.7.3.
27 June 2016	Protocol Amendment 2 Version 5: The investigational treatment continuation into subsequent cycle was updated to remove the need to have a creatinine clearance of at least 60 mL/min for subsequent cycles, since this was not required as per LEN SmPC. The target subject population/inclusion criteria (also reflected in Section 5.1 on study design and investigational plan). The need to have 60 mL/min at screening/baseline remained unchanged. EOT Visit added the need to perform an Unscheduled Visit, covering all the assessments for the EOT Visit after disease progression for patients who progressed but continued antibody therapy with MOR00208, at the discretion of the treating investigator. Corresponding text about this visit was added to several other places as applicable, including schedule of assessments. HBV serology was required monthly for all patients in the previous protocol version. This was changed to monthly only for those patients who had anti-HBc antibody positive (and HBV-DNA negative) at screening. Use of corticosteroids during study was elaborated and allowed short courses of corticosteroids for symptomatic relief. Repeated laboratory assessments during screening period was updated to allow one repeat of serum chemistry and haematology values in case of possible lab error, or due to temporarily abnormal lab values that could be attributed to a patient’s condition (e.g.dehydration) and could be corrected. Administrative changes to the Clinical Program Leader and change of the CRO including SAE reporting were also made.

23 October 2017	Protocol Amendment 3 Version 6: The antibody treatment with MOR00208 was extended beyond Cycle 24 until progression because the previous version of the protocol allowed an extended treatment with MOR00208 for subjects with an ongoing response of CR or PR for 24 cycles. The imaging frequency after Cycle 24 while on treatment with MOR00208 was amended to reduce the burden to subjects and investigators. Central Laboratory assessments to once a year were removed after Cycle 24 in order to simplify the study conduct. Change of sponsor signatories and change of sponsor address. Disease assessment by CT/MRI during additional treatment phase. Clarification of time points of scans during Cycle 13-24 was added. Schedule of assessments was adapted to be consistent with extended antibody treatment with MOR00208 beyond Cycle 24 until progression, imaging frequency after Cycle 24 while on treatment with MOR00208. Minor editorial changes and clarifications were updated. a)Data from previous ongoing and completed studies updated in Section 1.4.2 Safety of MOR00208. b) For subjects who were lost to follow-up, at least three attempts of contact by the site should have been made and documented in the source data c) Clarification of follow-up visits for OS occurring via telephone. d) Clarification of the name of the Drug Preparation Manual. e) Using actual body weight prior to each MOR00208 infusion was allowed, if this was preferred by investigators f) Clarification on treatment consisting of LEN and MOR00208 combination. This was administered up to twelve 28-day cycles at specified dose levels rather than until disease progression or discontinuation.
24 February 2021	Protocol Amendment 5 Version 8: The study duration per subject was at least 5 years including periods of screening (up to 28 days from signature of the Informed Consent Form (ICF), the treatment period (maximum 12 cycles for LEN + MOR00208 followed by MOR00208 monotherapy thereafter) and the survival follow-up phase. MOR00208 was administered until disease progression. The safety follow up period was extended to be allowed until the end of the study to provide important data on long term safety and survival outcomes. The end of the study (EOS) was defined as the date of the last visit of the last subject completing 5 years study duration including survival follow-up. If any subject was on treatment with MOR00208 at the end of the study and MOR00208 was not yet commercially available, subjects would be switched to alternative methods of supply with MOR00208. Upon study closure, MorphoSys would notify the applicable regulatory agencies in accordance with local requirements.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32511983