



## Clinical trial results:

**A phase II trial to evaluate the safety, feasibility and efficacy of a salvage therapy consisting of the mTOR inhibitor Temsirolimus (Torisel™) added to the standard therapy of Rituximab and DHAP for the treatment of patients with relapsed or refractory diffuse large cell B-Cell lymphoma – the STORM trial**

### Summary

EudraCT number	2011-001491-20
Trial protocol	DE
Global end of trial date	01 November 2018

### Results information

Result version number	v1 (current)
This version publication date	18 May 2022
First version publication date	18 May 2022
Summary attachment (see zip file)	STORM_Report (STORM_Ergebnisbericht_PharmNet.Bund_signed 20191023.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	STORM-2011
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01653067
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Ruprecht-Karls-University Heidelberg, Medical Faculty
Sponsor organisation address	INF , Heidelberg, Germany,
Public contact	Julia Meißner, Ruprecht-Karls University Heidelberg, Medical Faculty, 0049 6221568001, julia.meissner@med.uni-heidelberg.de
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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	01 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 October 2016
Global end of trial reached?	Yes
Global end of trial date	01 November 2018
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The STORM-trial consists of two parts.

In the part I (dose escalation of Temsirolimus) the primary objective is to establish a maximum tolerated dose of Temsirolimus in combination with Rituximab and DHAP.

In the part II (full target dose) the primary objective is to evaluate the ORR in patients with relapsed DLBCL.

Protection of trial subjects:

In a phase 1, a dose escalation was performed to establish a maximum tolerated dose of Temsirolimus in combination with Rituximab and DHAP.

Special attention in Part I and Part II of the study was brought to monitoring of adverse events. Frequency of Adverse events was calculated.

Background therapy:

All cohorts additionally received:

Rituximab (375 mg/m<sup>2</sup> day 2)

Dexamethasone 40 mg day 3-6

Cisplatin 100 mg/m<sup>2</sup> day 3

(Cisplatin could be replaced in the consecutive cycles by carboplatin AUC 5 if the patient experienced kidney toxicity in the previous cycle, i.e. decrease of creatinine clearance to 60 ml/min or lower.)

Evidence for comparator:

There was no comparator in this trial.

Actual start date of recruitment	31 January 2012
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	Germany: 53
Worldwide total number of subjects	53
EEA total number of subjects	53

Notes:

<b>Subjects enrolled per age group</b>	
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)	33
From 65 to 84 years	20
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Eligible patients with histologically proven diagnosis of DLBCL according to the World Health Organization classification and with first or second relapse of DLBCL were screened. After inclusion patients in part I of the trial received 2 to 4 cycles of 25 or 50 mg of Temsirolimus in combination with R-DHAP depending on the cohort were admitted.

### Pre-assignment

Screening details:

In total, 55 patients were assessed for eligibility. Fifty-three patients were enrolled, 15 patients in part I and 38 in part II of the study. Two patients were excluded from the study: 1 patient was identified as screening failure and another patient withdrew informed consent before start of treatment, respectively.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Part I 50 mg Temsirolimus

Arm description:

Part I (to examine dose limiting toxicity).

Part I was actually a separate period preceeding part II.

Arm type	examination of dose limiting toxicity
Investigational medicinal product name	Temsirolimus 50 mg
Investigational medicinal product code	L01E G01
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received 2 to 4 cycles of 50 mg of Temsirolimus

<b>Arm title</b>	Part I + II 25 mg Temsirolimus
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Arm description:

For the Part II proportion of the trial, Temsirolimus at 25mg on day 1 and 8 was determined as recommended dose following part I. Temsirolimus can be safely added to DHAP and Rituximab with promising activity.

Arm type	target dose (as established in part I)
Investigational medicinal product name	Temsirolimus 25 mg
Investigational medicinal product code	
Other name	Torisel
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received 2 to 4 cycles of 25 or 50 mg of Temsirolimus in combination with R-DHAP.

<b>Number of subjects in period 1</b>	Part I 50 mg Temsirrolimus	Part I + II 25 mg Temsirrolimus
Started	6	47
Completed	6	47

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment
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Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	53	53	
Age categorical			
Units: Subjects			
Adults (18-64 years)	33	33	
From 65-84 years	20	20	
Gender categorical			
Units: Subjects			
Female	20	20	
Male	33	33	

## End points

### End points reporting groups

Reporting group title	Part I 50 mg Temsirolimus
Reporting group description: Part I (to examine dose limiting toxicity). Part I was actually a separate period preceeding part II.	
Reporting group title	Part I + II 25 mg Temsirolimus
Reporting group description: For the Part II proportion of the trial, Temsirolimus at 25mg on day 1 and 8 was determined as recommended dose following part I. Temsirolimus can be safely added to DHAP and Rituximab with promising activity.	
Subject analysis set title	Total participants
Subject analysis set type	Full analysis
Subject analysis set description: All patients of phase 1 (25 mg) and 2 (50 mg)	

### Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR) <sup>[1]</sup>
End point description: In the part II (full target dose) the primary objective was the overall response rate in patients with relapsed DLBCL.	
End point type	Primary
End point timeframe: response at end of salvage therapy	

Notes:

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

Justification: No statistical tests have been performed in this single-arm study.

End point values	Part I 50 mg Temsirolimus	Part I + II 25 mg Temsirolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 <sup>[2]</sup>	47 <sup>[3]</sup>		
Units: Patients	4	32		

Notes:

[2] - 1 missing, 1 no overall response at end of follow-up

[3] - no overall response n= 13, missing n=2

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 30 days after the last dose of study drug or the start of new antineoplastic therapy within 30 days after STORM termination.

Adverse event reporting additional description:

All patients reported at least one AE. A total of 1678 AEs were reported (32 per pat.). Thereof, 253 AEs (15%, 42 per pat.) occurred in the group of patients treated with 50 mg Temsirolimus and 1425 AEs (85%, 30 per pat.) occurred in the group of patients treated with 25 mg Temsirolimus.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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### Reporting groups

Reporting group title	Total
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Reporting group description:

All patients included in this single-arm study

Serious adverse events	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 53 (81.13%)		
number of deaths (all causes)	21		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified	Additional description: Non-Hodgkin Lymphom		
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Vascular disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All AEs in this SOC		

subjects affected / exposed	6 / 53 (11.32%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	6 / 53 (11.32%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychiatric disorders	Additional description: Depression		
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Investigations	Additional description: All AEs in this SOC		
subjects affected / exposed	4 / 53 (7.55%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All AEs in this SOC		
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	3 / 53 (5.66%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			

Blood and lymphatic system disorders	Additional description: All SAEs in this SOC		
subjects affected / exposed	18 / 53 (33.96%)		
occurrences causally related to treatment / all	16 / 21		
deaths causally related to treatment / all	1 / 1		
Ear and labyrinth disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	3 / 53 (5.66%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	10 / 53 (18.87%)		
occurrences causally related to treatment / all	9 / 12		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders	Additional description: Angioedema		
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	13 / 53 (24.53%)		
occurrences causally related to treatment / all	6 / 16		
deaths causally related to treatment / all	0 / 0		
Infections and infestations	Additional description: All SAEs in this SOC		
subjects affected / exposed	10 / 53 (18.87%)		
occurrences causally related to treatment / all	11 / 12		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	5 / 53 (9.43%)		
occurrences causally related to treatment / all	5 / 6		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 53 (100.00%)		
Vascular disorders			
Vascular disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	20 / 53 (37.74%)		
occurrences (all)	25		
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All AEs in this SOC		
subjects affected / exposed	44 / 53 (83.02%)		
occurrences (all)	137		
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	34 / 53 (64.15%)		
occurrences (all)	70		
Psychiatric disorders			
Psychiatric disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	22 / 53 (41.51%)		
occurrences (all)	33		
Investigations			
Investigations	Additional description: All AEs in this SOC		
subjects affected / exposed	40 / 53 (75.47%)		
occurrences (all)	191		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All AEs in this SOC		
subjects affected / exposed	11 / 53 (20.75%)		
occurrences (all)	16		
Cardiac disorders			

Cardiac disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	11 / 53 (20.75%)		
occurrences (all)	18		
Nervous system disorders	Additional description: All AEs in this SOC		
Nervous system disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	43 / 53 (81.13%)		
occurrences (all)	104		
Blood and lymphatic system disorders	Additional description: All AEs in this SOC		
Blood and lymphatic system disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	51 / 53 (96.23%)		
occurrences (all)	486		
Ear and labyrinth disorders	Additional description: All AEs in this SOC		
Ear and labyrinth disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	14 / 53 (26.42%)		
occurrences (all)	18		
Eye disorders	Additional description: All AEs in this SOC		
Eye disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	15 / 53 (28.30%)		
occurrences (all)	17		
Gastrointestinal disorders	Additional description: All AEs in this SOC		
Gastrointestinal disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	48 / 53 (90.57%)		
occurrences (all)	242		
Skin and subcutaneous tissue disorders	Additional description: All AEs in this SOC		
Skin and subcutaneous tissue disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	28 / 53 (52.83%)		
occurrences (all)	47		
Renal and urinary disorders	Additional description: All AEs in this SOC		
Renal and urinary disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	23 / 53 (43.40%)		
occurrences (all)	29		
Endocrine disorders	Additional description: All AEs in this SOC		
Endocrine disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			

Musculoskeletal and connective tissue disorders	Additional description: All AEs in this SOC		
	subjects affected / exposed	21 / 53 (39.62%)	
	occurrences (all)	35	
Infections and infestations	Additional description: All AEs in this SOC		
	subjects affected / exposed	32 / 53 (60.38%)	
	occurrences (all)	53	
Metabolism and nutrition disorders	Additional description: All AEs in this SOC		
	subjects affected / exposed	41 / 53 (77.36%)	
	occurrences (all)	144	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2017	Change of principal investigator.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34589671>