



## Clinical trial results:

### Phase II study of thalidomide in combination with temozolomide in metastatic malignant melanoma with brain metastases

#### Summary

EudraCT number	2004-005164-25
Trial protocol	DK
Global end of trial date	04 December 2007

#### Results information

Result version number	v1 (current)
This version publication date	21 July 2021
First version publication date	21 July 2021

#### Trial information

##### Trial identification

Sponsor protocol code	04.09
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J. B. Winsløws vej 2, entrance 140, basement, Odense C, Denmark, 5000
Public contact	Ida Coordt Elle, Odense University Hospital, +45 29335922, ida.coordt.elle@rsyd.dk
Scientific contact	Lars Bastholt, Odense University Hospital, +45 24849408, lars.bastholt@rsyd.dk

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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	01 July 2008
Is this the analysis of the primary completion data?	No

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Global end of trial reached?	Yes
Global end of trial date	04 December 2007
Was the trial ended prematurely?	No

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Notes:

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**General information about the trial**

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Main objective of the trial:

To determine tumor response rate including determination of stable disease

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Protection of trial subjects:

Treatment with steroids if necessary.

Pre-medication to minimize adverse events.

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Background therapy: -

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Evidence for comparator: -

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Actual start date of recruitment	01 June 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Denmark: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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Notes:

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**Subjects enrolled per age group**

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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)	30
From 65 to 84 years	10
85 years and over	0

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## Subject disposition

### Recruitment

Recruitment details:

All patients included in the study had brain metastases in progression not amenable for surgery or stereotactic radiotherapy and due to limited symptoms whole brain radiotherapy was not indicated. WHO performance status (PS)  $\leq$  0.1.

### Pre-assignment

Screening details:

Forty screened patients were eligible and evaluable for response, and 39 were evaluable for toxicity. 25 patients had asymptomatic and 15 symptomatic brain metastases.

### Period 1

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

### Arms

Arm title	Tem-Thal
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Arm description:

TMZ in a dose of 150 mg/m<sup>2</sup> qd for seven days, followed by seven days off therapy and THA in 200 mg qd, both orally administered.

Arm type	Experimental
Investigational medicinal product name	Temozolomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

150 mg/m<sup>2</sup> qd for seven days, followed by seven days off therapy.

Investigational medicinal product name	Thalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Starting dose of THA was 100 mg qd orally, taken in the evening to reduce drug-related daytime somnolence. The dose was escalated after one week to a maximum of 200 mg qd given continuously.

<b>Number of subjects in period 1</b>	Tem-Thal
Started	40
Completed	40



## Baseline characteristics

### Reporting groups

Reporting group title	Trial
Reporting group description: -	

Reporting group values	Trial	Total	
Number of subjects	40	40	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	55		
full range (min-max)	29 to 76	-	
Gender categorical			
Patients in the trial.			
Units: Subjects			
Female	21	21	
Male	19	19	
Performance status			
Units: Subjects			
PS0	16	16	
PS1	24	24	

### Subject analysis sets

Subject analysis set title	Patients
Subject analysis set type	Full analysis

Subject analysis set description:

Forty screened patients were eligible and evaluable for response, and 39 were evaluable for toxicity. 25 patients had asymptomatic and 15 symptomatic brain metastases.

Reporting group values	Patients		
Number of subjects	40		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			

Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median full range (min-max)	55 29 to 76		
Gender categorical			
Patients in the trial.			
Units: Subjects			
Female	21		
Male	19		
Performance status Units: Subjects			
PS0	16		
PS1	24		

## End points

### End points reporting groups

Reporting group title	Tem-Thal
Reporting group description: TMZ in a dose of 150 mg/m <sup>2</sup> qd for seven days, followed by seven days off therapy and THA in 200 mg qd, both orally administered.	
Subject analysis set title	Patients
Subject analysis set type	Full analysis
Subject analysis set description: Forty screened patients were eligible and evaluable for response, and 39 were evaluable for toxicity. 25 patients had asymptomatic and 15 symptomatic brain metastases.	

### Primary: Response rate (CR+PR+SD)

End point title	Response rate (CR+PR+SD) <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: 12 months	
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: Please see attached publication for full statistical analysis.	

End point values	Tem-Thal	Patients		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	40	40		
Units: percent				
number (not applicable)				
Response rate	17.5	17.5		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

30 days post-last treatment

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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### Reporting groups

Reporting group title	Patients
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Reporting group description: -

Serious adverse events	Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 40 (47.50%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Lymphopenia	Additional description: Grade 3+4		
subjects affected / exposed	19 / 40 (47.50%)		
occurrences causally related to treatment / all	19 / 19		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 40 (92.50%)		
Vascular disorders			
Embolism	Additional description: Thrombo-embolism		
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	14 / 40 (35.00%)		
occurrences (all)	14		
Blood and lymphatic system disorders			



Lymphopenia subjects affected / exposed occurrences (all)	Additional description: Grade 1+2		
	13 / 40 (32.50%) 13		
General disorders and administration site conditions			
Dry mouth			
subjects affected / exposed	32 / 40 (80.00%)		
occurrences (all)	32		
Fatigue			
subjects affected / exposed	37 / 40 (92.50%)		
occurrences (all)	37		
Gastrointestinal disorders			
Anorexia			
subjects affected / exposed	20 / 40 (50.00%)		
occurrences (all)	20		
Constipation			
subjects affected / exposed	31 / 40 (77.50%)		
occurrences (all)	31		
Diarrhoea			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	7		
Nausea			
subjects affected / exposed	23 / 40 (57.50%)		
occurrences (all)	23		
Vomiting			
subjects affected / exposed	24 / 40 (60.00%)		
occurrences (all)	24		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	22 / 40 (55.00%)		
occurrences (all)	22		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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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/22275974>