Clinical trial results:
Safety of extended use of the weekly oral docetaxel formulation ModraDoc006/r in patients with advanced solid tumours

Summary

EudraCT number	2017-000347-41
Trial protocol	NL
Global end of trial date	16 July 2018

Results information

Result version number	v1 (current)
This version publication date	06 November 2022
First version publication date	06 November 2022

Trial information

Trial identification

Sponsor protocol code	N17DEX

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03150368
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Modra Pharmaceuticals
Sponsor organisation address	Barbara Strozzilaan 201, Amsterdam, Netherlands, 1083 HN
Public contact	M. Keessen, Modra Pharmaceuticals, 0031 0202050188, info@modrapharmaceuticals.com
Scientific contact	S. Marchetti, NKI-AVL, 0031 0205122446, s.marchetti@nki.nl

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	18 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2018
Global end of trial reached?	Yes
Global end of trial date	16 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety of extended use treatment with weekly ModraDoc006/r available for patients who completed treatment in one of the phase I trials with ModraDoc006/r, who might have clinical benefit of continued treatment with the oral docetaxel formulation.

Protection of trial subjects:

The study was conducted in accordance with the protocol, the current principles of the Declaration of Helsinki, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) requirements, the Medical Research Involving Human Subjects Act and any other applicable local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 May 2017
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	Netherlands: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	13
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Written informed consent was obtained before the start of any study related procedures. Patients had the right to withdraw from the study at any time, without giving an explanation and without prejudice to their subsequent care.

Pre-assignment

Screening details:

Screening assessments were done within 35 days before first dose according to the extended use program of ModraDoc006/r. In case of previous phase I studies with ModraDoc006/r with a duration of 4 weeks or less, the screening visit of this phase I study was used as screening visit for the present study (N17DEX).

Period 1

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

Arms

Arm title	ModraDoc006/r extension treatment

Arm description:

ModraDoc006/r is administered in patients who participated in other phase I trials with ModraD0c006/r at a similar dose regimen as in the previous ModraDoc006/r study.

Arm type	Experimental
Investigational medicinal product name	ModraDoc006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ModraDoc006 bi-daily once weekly (BIDW) 30 mg in the morning, and 20 mg in the evening

Investigational medicinal product name	ritonavir
Investigational medicinal product code	
Other name	Norvir®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ritonavir bi-daily once weekly (BIDW) 100 mg in the morning, and 100 mg in the evening

Number of subjects in period 1	ModraDoc006/r extension treatment
Started	17
Completed	17

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
Adults (18-64 years)	13	13	
From 65-84 years	4	4	
Age continuous Units: years			
median	58.8		
full range (min-max)	45 to 76	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	6	6	

End points

End points reporting groups

Reporting group title	ModraDoc006/r extension treatment

Reporting group description:

ModraDoc006/r is administered in patients who participated in other phase I trials with ModraD0c006/r at a similar dose regimen as in the previous ModraDoc006/r study.

Primary: Safety analysis

End point title	Safety analysis[1]

End point description:

To determine the safety of extended use treatment with weekly ModraDoc006/r in patients who completed treatment in one of the phase I trials with ModraDoc006/r, who might derive clinical benefit by continued treatment with the oral docetaxel formulation

End point type	Primary

End point timeframe:

Overall trial

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: In general, ModraDoc006/r was reasonably well tolerated. However, due to the low number of patients enrolled and the limited number of patients exposed for prolonged period of time to the study drug, no firm conclusions on the long-term safety of ModraDoc006/r should be drawn.

End point values	ModraDoc006/r extension treatment			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Subjects				
Patients reporting at least 1 TEAE	17			
Patients reporting drug related TEAEs	16			
Patients reporting serious TEAEs	8			
Patients reporting TEAEs leading to withdrawal	4			
Patients reporting TEAEs leading to death	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Toxicities were scored from the first study drug administration until the end of treatment visit.

Adverse event reporting additional description:

Toxicity was scored according to the CTC-AE (Common Terminology Criteria for Adverse Events, version 3.0).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Full analysis set

Reporting group description:

The full analysis set included all 17 enrolled patients. All patients received one or more doses of the study medication and are included in the per protocol analysis set and in the safety analysis set.

Serious adverse events	Full analysis set		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 17 (47.06%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Nausea			

subjects affected / exposed	4 / 17 (23.53%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Candida infection			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Full analysis set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Platelet count decreased			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	6		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 17 (29.41%)		
occurrences (all)	7		
Medical device site haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Eye disorders			
Scleral disorder			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	9 / 17 (52.94%)		
occurrences (all)	14		
Gastrointestinal inflammation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gingival pain			

subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Nausea subjects affected / exposed occurrences (all)	7 / 17 (41.18%) 15		
Rectal haemorrhage subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2		
Vomiting subjects affected / exposed occurrences (all)	5 / 17 (29.41%) 17		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Dry skin subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Onychomadesis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Infections and infestations Candida infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported