

**Clinical trial results:****Phase II study of Irofulven in AR-targeted and Docetaxel-Pretreated Metastatic Castration-Resistant Prostate Cancer Patients, who have a Drug Response Predictor (DRP™) indicating a high likelihood of response to Irofulven****Summary**

EudraCT number	2017-003549-72
Trial protocol	DK
Global end of trial date	01 June 2022

**Results information**

Result version number	v1 (current)
This version publication date	03 October 2024
First version publication date	03 October 2024

**Trial information****Trial identification**

Sponsor protocol code	SMR-3165
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03643107
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	Allarity Therapeutics Europe ApS
Sponsor organisation address	Venlighedsvej 1, Herlev, Denmark, 2970
Public contact	Gedske Daugaard, Rigshospitalet, +45 3545 1125, mfoegh@allarity.com
Scientific contact	Gedske Daugaard, Rigshospitalet, +45 3545 1125, mfoegh@allarity.com
Sponsor organisation name	Allarity Therapeutics Europe ApS
Sponsor organisation address	Venlighedsvej 1, Herlev, Denmark, 2970
Public contact	Jeremy Graff, Allarity Therapeutics ApS, NA NA, jgraff@allarity.com
Scientific contact	Jeremy Graff, Allarity Therapeutics ApS, NA NA, jgraff@allarity.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	Final
Date of interim/final analysis	10 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2022
Global end of trial reached?	Yes
Global end of trial date	01 June 2022
Was the trial ended prematurely?	No

Notes:

### General information about the trial

Main objective of the trial:

To evaluate the anti-tumour effect after treatment with 0.45mg/kg Irofulven in combination prednisolone in patients who progressed on AR-targeted therapy (abiraterone acetate, enzalutamide or investigational AR-targeted agent) and docetaxel-pretreated metastatic castration-resistant prostate cancer and that were selected by the Irofulven DRP.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, adopted by the 18th World Medical Association (WMA) General Assembly, Helsinki, Finland, June 1964, and subsequent amendments and International Council for Harmonisation (ICH) guideline for Good Clinical Practice E6 (R1)(European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use CHMP)/ICH/135/1995), including archiving of essential documents and the EU Clinical Trial Directive (CTD)2001/20/EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2018
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	Denmark: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	2
From 65 to 84 years	8
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited at 2 sites in Denmark.

### Pre-assignment

Screening details:

A drug response prediction (DRP) was used as a companion diagnostic for selection of patients.

### Period 1

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

Blinding implementation details:

Open trial.

### Arms

<b>Arm title</b>	Irofulven treatment
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Arm description:

0.45mg/kg Irofulven at day 1 in 3-week cycle.

Arm type	Experimental
Investigational medicinal product name	Irofulven
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.45 mg/kg (limited to 50 mg total dose) at day 1 of a 3 week cycle.

<b>Number of subjects in period 1</b>	Irofulven treatment
Started	10
Completed	10

## Baseline characteristics

## End points

### End points reporting groups

Reporting group title	Irofulven treatment
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Reporting group description:

0.45mg/kg Irofulven at day 1 in 3-week cycle.

### Primary: Clinical benefit rate

End point title	Clinical benefit rate <sup>[1]</sup>
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End point description:

Anti-tumor effect of Irofulven with prednisolone on clinical benefit rate (CBR) defined as complete response or partial response > 9 weeks according to RECIST 1.1 for patients with measurable disease and defined as stable disease > 9 weeks according to PCWG3 for bone metastases.

End point type	Primary
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End point timeframe:

First dose until progression

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: Not applicable

End point values	Irofulven treatment			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Patients				
Clinical benefit	0			
No clinical benefit	10			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose until 28 days after last dose.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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### Reporting groups

Reporting group title	All subjects
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Reporting group description: -

<b>Serious adverse events</b>	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Coronary artery occlusion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocarditis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Small intestinal obstruction subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders Hydronephrosis subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations Device related infection subjects affected / exposed	1 / 10 (10.00%)		
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 %

<b>Non-serious adverse events</b>	All subjects		
Total subjects affected by non-serious adverse events subjects affected / exposed	9 / 10 (90.00%)		
Vascular disorders Phlebitis subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Surgical and medical procedures Orchidectomy subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
General disorders and administration site conditions Fatigue subjects affected / exposed	8 / 10 (80.00%)		
occurrences (all)	8		
Oedema peripheral subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
peripheral sw			

<p>subjects affected / exposed occurrences (all)</p> <p>Pyrexia subjects affected / exposed occurrences (all)</p>	<p>1 / 10 (10.00%) 1</p> <p>1 / 10 (10.00%) 1</p>		
<p>Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)</p>	<p>1 / 10 (10.00%) 1</p>		
<p>Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)</p> <p>Dyspnoea subjects affected / exposed occurrences (all)</p> <p>Epistaxis subjects affected / exposed occurrences (all)</p> <p>Pneumonitis subjects affected / exposed occurrences (all)</p>	<p>2 / 10 (20.00%) 2</p> <p>4 / 10 (40.00%) 4</p> <p>1 / 10 (10.00%) 1</p> <p>1 / 10 (10.00%) 1</p>		
<p>Investigations Neutrophil count decreased subjects affected / exposed occurrences (all)</p> <p>Platelet count decreased subjects affected / exposed occurrences (all)</p> <p>Weight decreased subjects affected / exposed occurrences (all)</p> <p>White blood cell count decreased subjects affected / exposed occurrences (all)</p>	<p>1 / 10 (10.00%) 1</p> <p>4 / 10 (40.00%) 4</p> <p>4 / 10 (40.00%) 4</p> <p>2 / 10 (20.00%) 2</p>		
<p>Cardiac disorders</p>			

Myocarditis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Headache subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Myasthenia gravis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Neuralgia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Spinal cord compression subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	4 / 10 (40.00%) 4		
Neutropenia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Eye disorders Diplopia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		

Dry eye subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3		
Photophobia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Photopsia subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3		
Retinopathy subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Vision blurred subjects affected / exposed occurrences (all)	4 / 10 (40.00%) 4		
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	6 / 10 (60.00%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3		
Nausea subjects affected / exposed occurrences (all)	6 / 10 (60.00%) 6		
Vomiting subjects affected / exposed occurrences (all)	4 / 10 (40.00%) 4		
Skin and subcutaneous tissue disorders			
Night sweats subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Renal and urinary disorders			
Nocturia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Muscle tightness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2018	Substantial modification of the protocol. Change related to inclusion/exclusion criteria.
26 October 2018	Substantial amendment of protocol. A change in the primary efficacy variable was implemented.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported