



Clinical trial results:

A Modular Phase II, Open-Label, Multicentre Study to Assess the Efficacy and Safety of Capivasertib in Patients with Relapsed or Refractory B-cell Non-Hodgkin Lymphoma (CAPITAL)

Summary

EudraCT number	2021-000870-27
Trial protocol	FR ES DK
Global end of trial date	25 October 2024

Results information

Result version number	v1 (current)
This version publication date	08 December 2024
First version publication date	08 December 2024

Trial information

Trial identification

Sponsor protocol code	D361FC00001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05008055
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical study Information Center
Sponsor organisation address	Södertälje, Södertälje, Sweden, 151 85
Public contact	AstraZeneca Clinical Study Information Center, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.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	22 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 August 2023
Global end of trial reached?	Yes
Global end of trial date	25 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate the effectiveness of the module-defined study treatment by assessment of objective response rate (ORR) based on Lugano 2014 Classification response criteria in each cohort as determined by blinded independent central review (BICR).

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics and Human Biological Samples

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2021
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	Canada: 2
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	30
EEA total number of subjects	13

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)	15
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 3 November 2021 and analyses presented in this results form are based on a data cut-off of 22 August 2023.

Pre-assignment

Screening details:

Patients who met the inclusion and none of the exclusion criteria were enrolled to the study. This study consisted of a screening period of 28 days. All the study assessments were performed as per schedule of assessment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	R/R FL: Capiwasertib monotherapy

Arm description:

Patients with Relapsed or refractory Follicular Lymphoma (R/R FL) received capivasertib 480 mg orally until progression of disease (PD) or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.

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

Dosage and administration details:

Capivasertib was taken at 480 mg orally twice a day (BD) until disease progression or unacceptable toxicity.

Arm title	R/R MZL: Capivasertib monotherapy
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Arm description:

Patients with Relapsed or refractory Marginal zone lymphoma (R/R MZL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.

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

Dosage and administration details:

Capivasertib was taken at 480 mg orally BD until disease progression or unacceptable toxicity.

Arm title	R/R MCL: Capivasertib monotherapy
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Arm description:

Patients with Relapsed or refractory Mantle cell lymphoma (R/R MCL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.

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

Dosage and administration details:

Capivasertib was taken at 480 mg orally BD until disease progression or unacceptable toxicity.

Number of subjects in period 1	R/R FL: Capivasertib monotherapy	R/R MZL: Capivasertib monotherapy	R/R MCL: Capivasertib monotherapy
Started	16	4	10
Completed	13	3	9
Not completed	3	1	1
Patients ongoing treatment as of 22 August 2023.	3	1	1

Baseline characteristics

Reporting groups

Reporting group title	R/R FL: Capiwasertib monotherapy
Reporting group description: Patients with Relapsed or refractory Follicular Lymphoma (R/R FL) received capivasertib 480 mg orally until progression of disease (PD) or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.	
Reporting group title	R/R MZL: Capiwasertib monotherapy
Reporting group description: Patients with Relapsed or refractory Marginal zone lymphoma (R/R MZL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.	
Reporting group title	R/R MCL: Capiwasertib monotherapy
Reporting group description: Patients with Relapsed or refractory Mantle cell lymphoma (R/R MCL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.	

Reporting group values	R/R FL: Capiwasertib monotherapy	R/R MZL: Capiwasertib monotherapy	R/R MCL: Capiwasertib monotherapy
Number of subjects	16	4	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	1	2
From 65-84 years	4	3	7
85 years and over	0	0	1
Age Continuous Units: Years			
arithmetic mean	55.7	66.8	76.2
standard deviation	± 12.07	± 4.92	± 9.72
Sex: Female, Male Units: Participants			
Female	7	2	4
Male	9	2	6
Race, Customised Units: Subjects			
Asian	5	0	0
White	10	3	7
Other	0	1	1
Not reported	1	0	2
Ethnicity, Customised Units: Subjects			
Hispanic or Latino	3	0	0
Not Hispanic or Latino	12	4	5

Missing	0	0	4
Other	1	0	1

Reporting group values	Total		
Number of subjects	30		
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)	15		
From 65-84 years	14		
85 years and over	1		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	13		
Male	17		
Race, Customised Units: Subjects			
Asian	5		
White	20		
Other	2		
Not reported	3		
Ethnicity, Customised Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	21		
Missing	4		
Other	2		

End points

End points reporting groups

Reporting group title	R/R FL: Capiwasertib monotherapy
Reporting group description: Patients with Relapsed or refractory Follicular Lymphoma (R/R FL) received capivasertib 480 mg orally until progression of disease (PD) or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.	
Reporting group title	R/R MZL: Capiwasertib monotherapy
Reporting group description: Patients with Relapsed or refractory Marginal zone lymphoma (R/R MZL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.	
Reporting group title	R/R MCL: Capiwasertib monotherapy
Reporting group description: Patients with Relapsed or refractory Mantle cell lymphoma (R/R MCL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.	

Primary: Objective response rate

End point title	Objective response rate ^[1]
End point description: Objective response rate is defined as the proportion of patients achieving either complete response (CR) or partial response (PR) according to the Lugano 2014 Classification for non-Hodgkin lymphoma (NHL) as assessed by blinded independent central review (BICR). The endpoint included response evaluable analysis set which included all patients, treated with study treatment, with measurable disease at baseline.	
End point type	Primary
End point timeframe: First dose until progression of disease [PD] or last evaluable assessment in the absence of progression or data cut-off date (21.6 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: No statistical analysis was performed.	

End point values	R/R FL: Capiwasertib monotherapy	R/R MZL: Capiwasertib monotherapy	R/R MCL: Capiwasertib monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	3	10	
Units: Percentage of Patients				
number (confidence interval 95%)	18.8 (4.0 to 45.6)	33.3 (0.8 to 90.6)	30.0 (6.7 to 65.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response
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End point description:

Duration of response is defined as the time from the date of first documented response until date of documented progression according to the Lugano 2014 Classification for NHL as assessed by BICR, or death due to any cause. The arbitrary value 9999.9999, and 0.9999 represents data that data were not calculable due to a low number of patients. The endpoint included response evaluable analysis set which included all patients, treated with study treatment, with measurable disease at baseline.

End point type	Secondary
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End point timeframe:

First documented response until date of documented progression or data-cut off date (21.6 Months)

End point values	R/R FL: Capiwasertib monotherapy	R/R MZL: Capiwasertib monotherapy	R/R MCL: Capiwasertib monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	3	
Units: Months				
median (confidence interval 95%)	1.9 (1.7 to 9999.9999)	9999.9999 (9999.9999 to 9999.9999)	1.9 (0.9999 to 9999.9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival
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End point description:

Progression-free survival is defined as the time from the date of first dose until documented disease progression according to the Lugano 2014 Classification for NHL as assessed by BICR, or death due to any cause. The analysis included all dosed patients, regardless of whether the patient withdrew from therapy, received another anti lymphoma therapy, or clinically progressed prior to progression according to the Lugano 2014 Classification for NHL. The arbitrary value 9999.9999 represents that upper limit of the 95% confidence interval (CI) was not reached due to the insufficient number of patients with events, and the short duration of follow-up. The endpoint included safety analysis set which included all patients who received any amount of study treatment.

End point type	Secondary
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End point timeframe:

First dose until documented disease progression or data cut-off date (21.6 Months)

End point values	R/R FL: Capiwasertib monotherapy	R/R MZL: Capiwasertib monotherapy	R/R MCL: Capiwasertib monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	4	10	
Units: Months				
median (confidence interval 95%)	5.4 (3.4 to 9999.9999)	9999.9999 (1.4 to 9999.9999)	1.9 (0.9 to 9999.9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
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End point description:

Overall survival is defined as time from the date of first dose until the date of death due to any cause. The analysis included all dosed patients, regardless of whether the patient withdrew from therapy or received another anti lymphoma therapy. Patients who had not died by the analysis DCO date were censored at their last known date of being alive before the DCO date. Patients who were known to be alive or dead after the DCO date were censored at the DCO date. Patients who were lost to follow-up were censored at the date when they were last known to have been alive. The arbitrary value 9999.9999 represents that median, and 95% CI could not be calculated as no patients were seen to experience the event of interest due to short duration of follow-up, and as they were not reached. The endpoint included safety analysis set which included all patients who received any amount of study treatment.

End point type	Secondary
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End point timeframe:

First dose until data cut-off date (21.6 Months)

End point values	R/R FL: Capiwasertib monotherapy	R/R MZL: Capiwasertib monotherapy	R/R MCL: Capiwasertib monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	4	10	
Units: Months				
median (confidence interval 95%)	9999.9999 (9999.9999 to 9999.9999)	9999.9999 (1.4 to 9999.9999)	9999.9999 (2.0 to 9999.9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with adverse events and serious adverse events

End point title	Number of patients with adverse events and serious adverse events
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End point description:

The safety and tolerability of the capivasertib treatment in each Cohort was assessed.

End point type	Secondary
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End point timeframe:

Screening (Day -28 to -1) until Post-treatment follow-up up to 30 days after last dose or long-term follow-up or study completion (Every 12 weeks until death or lost to follow-up, unless patient have withdrawn consent [up to 21.6 Months])

End point values	R/R FL: Capivasertib monotherapy	R/R MZL: Capivasertib monotherapy	R/R MCL: Capivasertib monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	4	10	
Units: Participants				
Any adverse event (AE)	16	3	10	
Any AE possibly related to treatment	14	3	8	
Any AE of CTCAE grade 3 or higher	7	1	7	
CTCAE \geq grade 3 AEs, possibly treatment-related	3	1	5	
Any AE with outcome = death	0	0	0	
Possibly treatment-related AE with outcome = death	0	0	0	
Any SAE (including events with outcome = death)	2	0	3	
Possibly treatment-related SAEs (including deaths)	0	0	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of capivasertib overtime

End point title	Plasma concentration of capivasertib overtime
End point description:	
The plasma concentration of capivasertib when administered in patients in each Cohort was determined. The arbitrary value 9999.9999 represents that geometric mean was not quantified because in given time point, when less than or equal to 50% of the concentration values were not measurable or quantified. The endpoint included pharmacokinetic (PK) analysis set which included all patients who received at least 1 dose of capivasertib, for whom there is at least 1 reportable PK concentration. CTCAE: Common Terminology Criteria for Adverse Events.	
End point type	Secondary
End point timeframe:	
Cycle 1 (28-day treatment Cycle) Day 1 and on Cycle 1 Day 8, Cycle 1 Day 15 and Cycle 1 Day 22 (Pre-dose and post-dose)	

End point values	R/R FL: Capivasertib monotherapy	R/R MZL: Capivasertib monotherapy	R/R MCL: Capivasertib monotherapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	4	9	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (Post-dose [1 hour])	394.9 (\pm 157.0)	414.4 (\pm 125.7)	287.1 (\pm 676.2)	

Cycle 1 Day 1 (Post-dose [2 hours])	883.7 (± 59.12)	962.9 (± 40.33)	976.1 (± 58.27)	
Cycle 1 Day 1 (Post-dose [4 hours])	528.5 (± 49.28)	677.2 (± 65.77)	780.1 (± 56.99)	
Cycle 1 Day 8 (Pre-dose)	6.149 (± 207.4)	8.477 (± 103.9)	14.31 (± 138.8)	
Cycle 1 Day 15 (Pre-dose)	5.844 (± 146.1)	9.245 (± 73.63)	32.36 (± 373.5)	
Cycle 1 Day 22 (Pre-dose)	7.974 (± 372.2)	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening (Day -28 to -1) until Post-treatment follow-up up to 30 days after last dose or long-term follow-up or study completion (Every 12 weeks until death or lost to follow-up, unless patient have withdrawn consent [up to 21.6 Months])

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	R/R FL: Capivasertib monotherapy
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Reporting group description:

Patients with Relapsed or refractory Follicular Lymphoma (R/R FL) received capivasertib 480 mg orally until progression of disease (PD) or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.

Reporting group title	R/R MCL: Capivasertib monotherapy (Experimental)
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Reporting group description:

Patients with Relapsed or refractory Mantle cell lymphoma (R/R MCL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.

Reporting group title	R/R MZL: Capivasertib monotherapy
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Reporting group description:

Patients with Relapsed or refractory Marginal zone lymphoma (R/R MZL) received capivasertib 480 mg orally until PD or unacceptable toxicity, or if the patient/investigator requests to stop the treatment.

Serious adverse events	R/R FL: Capivasertib monotherapy	R/R MCL: Capivasertib monotherapy (Experimental)	R/R MZL: Capivasertib monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 16 (12.50%)	3 / 10 (30.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	2	1
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Obliterative bronchiolitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	R/R FL: Capiwasertib monotherapy	R/R MCL: Capiwasertib monotherapy (Experimental)	R/R MZL: Capiwasertib monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	9 / 10 (90.00%)	3 / 4 (75.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Orthostatic hypotension			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Peripheral swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Fatigue			
subjects affected / exposed	3 / 16 (18.75%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	5	2	0
Oedema peripheral			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Haemoptysis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Investigations Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 2	0 / 4 (0.00%) 0
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0

Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Anosmia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	3 / 16 (18.75%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	4	0	1
Memory impairment			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Neutrophilia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	3 / 16 (18.75%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Lymphocytosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Ocular discomfort subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Gastrointestinal disorders			
Dental caries subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	15 / 16 (93.75%) 29	4 / 10 (40.00%) 8	2 / 4 (50.00%) 3
Dry mouth subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Intussusception subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	5 / 10 (50.00%) 6	2 / 4 (50.00%) 2
Odynophagia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Proctalgia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	1 / 4 (25.00%) 1
Vomiting			

subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 10 (10.00%) 2	1 / 4 (25.00%) 1
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Hypertransaminaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Rash			
subjects affected / exposed	2 / 16 (12.50%)	3 / 10 (30.00%)	0 / 4 (0.00%)
occurrences (all)	2	7	0
Rash maculo-papular			
subjects affected / exposed	2 / 16 (12.50%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	6	0	0
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	2 / 16 (12.50%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	1

Musculoskeletal discomfort subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 4	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Respiratory tract infection viral subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 10 (0.00%) 0	1 / 4 (25.00%) 1
Herpes zoster subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Cystitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	1 / 4 (25.00%) 1
Wound abscess subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Escherichia urinary tract infection subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Metabolism and nutrition disorders			
Dehydration subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 10 (10.00%) 3	0 / 4 (0.00%) 0
Glucose tolerance impaired			

subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	3	0
Hyperuricaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Hypokalaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Decreased appetite			
subjects affected / exposed	2 / 16 (12.50%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	2	2	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 April 2021	Amendment 01: Exclusion criteria amended to exclude patients with increased risk of venous thromboembolism (VTE) not willing to receive VTE prophylaxis and to exclude the concomitant use of UGT2B7 inhibitors/inducers. Additional information added on dietary restrictions with capivasertib. Module I updated: to include further details on the selection of the dose for capivasertib monotherapy and to provide the rationale for the proposed intermittent dosing schedule. Inclusion criteria updated to include the current need for systemic treatment and to clarify that all patients (with FL, MZL, or MCL depending upon Cohort) must have had relapsed, progressed, or be refractory after at least 2 prior lines of systemic therapy instead of one. Exclusion criterion updated to exclude patients with an immediate need for cytoreductive treatment.
28 July 2021	Amendment 02: In Module I inclusion criteria updated to clarify that physicians should discuss CAR-T cell therapy for R/R FL and MCL patients prior to study enrolment.
24 February 2022	Amendment 03: Inclusion criterion number 6 updated to clarify that the pregnancy test should be done on a serum sample. Text added regarding bone marrow aspirates/biopsy performed as part of standard of care and up to 12 weeks prior to informed consent form signature. Removal of urinary tract infection, pneumonia, and Torsades de pointes from the AESI list. Addition of infective pneumonia. Updated in line with current list of AESIs for capivasertib. Inclusion criteria updated to delete text stating the maximum number of prior lines of therapy (for patients with R/R FL, MZL, or MCL depending upon Cohort).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported