Clinical trial results:
Peptide vaccination with PD-L1 and PD-L2 peptides in untreated chronic lymphatic leukemia.

Summary

EudraCT number	2018-004869-14
Trial protocol	DK
Global end of trial date	15 March 2022

Results information

Result version number	v1 (current)
This version publication date	16 September 2022
First version publication date	16 September 2022

Trial information

Trial identification

Sponsor protocol code	CLL19H1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Herlev Hospital
Sponsor organisation address	Borgmester Ib Juuls Vej 1, Herlev, Denmark, 2730
Public contact	Primary invetsigator, Dept. of hematology, Herlev Hospital, 0045 38689210, uffe.klausen@regionh.dk
Scientific contact	Primary invetsigator, Dept. of hematology, Herlev Hospital, 0045 38689210, uffe.klausen@regionh.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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 March 2022
Global end of trial reached?	Yes
Global end of trial date	15 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to evaluate the efficacy of the vaccine, in means of changes in the lymphocyte count and structural changes in lymph node and/or spleen size.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 19
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	6
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Due to stop in recruitments with the arrival of the COVID-19 pandemic, 19 out of intended 20 patients were included from May 2019 to February 2020.

Pre-assignment

Screening details:

All patients meeting the inclusion and exclusion criteria were recruited except one patient who redrew consent.

Period 1

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

Arms

Arm title	Treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	PD-L1 and PD-L2 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 ug PD-L1 peptide and 100 ug PD-L2 peptide dissolved in 10 % DMSO, 40% water and 50% Montanide ISA 51 with a total volume of 1 ml.

Number of subjects in period 1	Treatment
Started	19
Completed	17
Not completed	2
Adverse event, serious fatal	1
Lack of efficacy	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	19	19	
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	70		
full range (min-max)	53 to 81	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	12	12	

Subject analysis sets

Subject analysis set title	Population
Subject analysis set type	Full analysis

Subject analysis set description:
Studypopulation

Reporting group values	Population		
Number of subjects	19		
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)	 70 53 to 81		
Gender categorical Units: Subjects			
Female Male	7 12		

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: -	
Subject analysis set title	Population
Subject analysis set type	Full analysis
Subject analysis set description: Studypopulation	

Primary: Clinical response

End point title	Clinical response[1]
End point description:	
End point type	Primary
End point timeframe: At end of treatment (0-24 months from recruitment) no patients achieved responses meeting the criteria defined by the international working group on CLL.	

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: Descriptive

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Paticipants				
Complete remission	0			
Partial response	0			
Stable disease	17			
Progressive disease	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Immune response measured by elispot

End point title	Immune response measured by elispot
End point description:	
End point type	Secondary
End point timeframe: Measured at baseline and after three, six and nine vaccines.	

End point values	Treatment	Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	17	17		
Units: Number of patients with response				
PDL1 responses	13	13		
PD-L2 responses	15	15		

Attachments (see zip file)	Response table/table for EU.PNG

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4

Reporting groups	
Reporting group title	Study population

Reporting group description: -

Serious adverse events	Study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 19 (36.84%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Facial nerve disorder			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Autoimmune anaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
elevated creatinine			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Viral infection			
subjects affected / exposed	1 / 19 (5.26%)		
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 %

Non-serious adverse events	Study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 19 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
lung cancer			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Prostate cancer			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Vascular disorders			
Thromboflebitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

General disorders and administration site conditions			
Chills			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	7		
Fatigue			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Injection site reaction			
subjects affected / exposed	9 / 19 (47.37%)		
occurrences (all)	16		
Nausea			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Night sweats			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	3		
Vertigo			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
upper airway infection			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	4		
Bronchospasm			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	5		
Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Cough			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Sinuitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Nervous system disorders			
dizzyness			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hyperalgesia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
paresthesia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
adenit			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Anemia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
facial edema			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Pseudohyperkalaemia			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
diarrhea			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Gastroenteritis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Ileus			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Bullous dermatitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	3		
Granuloma			
subjects affected / exposed	7 / 19 (36.84%)		
occurrences (all)	9		
shingles			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Rosacea			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Skin infection			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Renal and urinary disorders			
Polyuria			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Endocrine disorders			
Hypercalcemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Bursitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	4		
Myositis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
tendovaginitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Infections and infestations			
bladder infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	4		

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