Clinical trial results:
Phase IIa trial of PD-L1 peptide vaccination as monotherapy in high risk smoldering multiple myeloma

Summary

EudraCT number	2018-003990-93
Trial protocol	DK
Global end of trial date	10 March 2021

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	MY18H2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03850522
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	Clinical Trial Information, Center for Cancer Immune Therapy, Department of Hematology, Herlev and Gentofte University Hospital, nicolai.groenne.dahlager.joergensen.01@regionh.dk
Scientific contact	Clinical Trial Information, Center for Cancer Immune Therapy, Department of Hematology, Herlev and Gentofte University Hospital, nicolai.groenne.dahlager.joergensen.01@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	10 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 March 2021
Global end of trial reached?	Yes
Global end of trial date	10 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the phase IIa trial is to investigate the rate of response in patients with high risk smoldering multiple myeloma vaccinated with PD-L1 long1. Furthermore, immunogenicity of the vaccine, adverse events, quality of life, time to progression and overall survival will be described.

Hypothesis: Ten vaccinations with the peptide PD-L1 long1 will lead to a decline of 50% or more of the M-component or involved free light chain measured in the blood of patients with high risk smoldering multiple myeloma two weeks after last vaccination.

Protection of trial subjects:

The patient will be observed for acute reactions for 15 minutes after the vaccination, where pulse and blood pressure will be measured prior to the vaccination and before the patient leaves the outpatient clinic. Pain during administration can be handled with mild analgesic such as 500-1000 mg paracetamol. If acute reactions occur, the patient will be treated according to guidelines and the patient will be excluded if the reaction is serious. Regarding exclusion due to acute reactions, vasovagal reactions are not considered as acute and must be ruled out.

Safety will be evaluated on basis of symptoms reported by the participating patients as well as assessed with laboratory parameters from e.g. blood samples and ECG.
Methods and timing for assessment, recording and analysis of safety parameters
Adverse events will be recorded from first vaccination until the end-of-study visit two weeks after last the vaccine.

In relation with each visit with vaccination, the patient will be questioned about new symptoms since last vaccination or changes in symptoms since last vaccination. If the patient has symptoms, the health professional responsible for the visit (whether it is a nurse trained for the study or a sub investigator) will record symptoms in the patient’s electronic health records and record adverse events according to CTCAE version 4.03 in the CTC-file. The questioning about symptoms can be performed at the physical visit or by telephone up to 48 hours before the vaccination.
The vaccine will be given by a nurse trained for giving the vaccine in this trial or by a sub investigator or the primary investigator.
The patients will be asked to complete the PRO-CTCAE questionnaire, specifically designed to capture symptomatic toxicities from the PD-L1 vaccines as experienced in the phase I study of the PD-L1 vaccine as well as literature review. Also, the PRO-CTCAE contains the possibility for patients themselves to describe any unexpected symptomatic toxicities

Background therapy:

None

Standard of care is observation.

Evidence for comparator: -

Actual start date of recruitment	18 February 2019
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: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	3
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Since high risk smoldering multiple myeloma is a rare disease, enrollment of more than 10 patients can be challenged by incoming competing trials, the study will be closed after 1,5 years.
Patients will be recruited from the departments of hematology in Denmark. Smoldering multiple myeloma and a maximum of 5 years after diagnosis.

Pre-assignment

Screening details:

29 patients were screened.

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	Vaccination

Arm description:

500 µl aqueous solution of 100µg PD-L1 long1 peptide dissolved in DMSO and PBS is mixed to an emulsion with 500µl Montanide ISA-51, given subcutaneously every second week for a total of 10 vaccinations per patient. If the investigator deems that the patient is benefitting from vaccinations, the patient can continue in the extension phase of the study and receive up to 20 additional vaccinations. In the extension phase of the study, the frequency of vaccinations can be increased to weekly and several treatment pauses can be inserted.

Arm type	Experimental
Investigational medicinal product name	IO103
Investigational medicinal product code	
Other name	PD-L1 long1
Pharmaceutical forms	Emulsion for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IO103 drug product is a freeze dried powder to be dissolved DMSO and in water for injection. The solution is administered subcutaneously after mixing with adjuvant (Montanide ISA 51 VG).

A 500 µl aqueous solution of 100µg PD-L1 long1 peptide dissolved in DMSO and PBS is mixed to an emulsion with 500µl Montanide ISA-51 and given as a subcutaneous injection on the lateral side of the upper arm preceded by disinfection.

Number of subjects in period 1	Vaccination
Started	6
Completed	5
Not completed	1
Physician decision	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	3	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	3	3	

End points

End points reporting groups

Reporting group title	Vaccination

Reporting group description:

500 µl aqueous solution of 100µg PD-L1 long1 peptide dissolved in DMSO and PBS is mixed to an emulsion with 500µl Montanide ISA-51, given subcutaneously every second week for a total of 10 vaccinations per patient. If the investigator deems that the patient is benefitting from vaccinations, the patient can continue in the extension phase of the study and receive up to 20 additional vaccinations. In the extension phase of the study, the frequency of vaccinations can be increased to weekly and several treatment pauses can be inserted.

Primary: Overall response rate

End point title	Overall response rate[1]

End point description:

Patients with a response according to the IMWG criteria as PR+VGPR+CR+sCR during treatment and two weeks after end of treatment per patient.

End point type	Primary

End point timeframe:

Planned analysis cut-off per patient: two weeks after last vaccination

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 analyses were performed on this endpoint.

End point values	Vaccination			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: response	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion until two weeks after last vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Vaccination

Reporting group description:

500 µl aqueous solution of 100µg PD-L1 long1 peptide dissolved in DMSO and PBS is mixed to an emulsion with 500µl Montanide ISA-51, given subcutaneously every second week for a total of 10 vaccinations per patient. If the investigator deems that the patient is benefitting from vaccinations, the patient can continue in the extension phase of the study and receive up to 20 additional vaccinations. In the extension phase of the study, the frequency of vaccinations can be increased to weekly and several treatment pauses can be inserted.

Serious adverse events	Vaccination		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Vaccination		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Immune system disorders			
Flu-like symptoms after vaccination	Additional description: One patient had grade 1 to 2 flu-like symptoms after most vaccinations.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	22		
Gastrointestinal disorders			
Bloating	Additional description: Mild bloating and gastrointestinal dyscomfort. 1 patient, grade 2, 2 days. Known for the patient, not different from other frequent occurences for the patient previously.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Diverticulitis	Additional description: 1 patient, grade 2, 16 days till last symptom. A known recurrent problem for the patient, not different from previous occurrences.		

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Sore throat	Additional description: Grade 2 in one patient, lasted 2 days.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Injection site reaction			
subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	30		
Musculoskeletal and connective tissue disorders			
Bursitis	Additional description: Bursitis olecrani, 1 patient, grade 2, lasted 5 days. Has had it previously.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infections and infestations			
Viral infektion	Additional description: Grade 2 viral infektion, one patient, lasting 2 days.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Otitis media	Additional description: 1 patient, lasting 2 days, the patient is known with recurring otitis media, this occurence was no different than the cases the patient has had many times.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2019	Possibility to extend the planned 10 vaccinations to an additional up to 20 vaccines in patients deemed to have effect of the vaccine.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported