Clinical trial results:
Toll-like receptor 9 enhancement of antiviral immunity in chronic HIV-1 infection: a phase 1b/2a trial (TEACH)

Summary

EudraCT number	2014-005634-59
Trial protocol	DK
Global end of trial date	06 December 2017

Results information

Result version number	v1 (current)
This version publication date	05 December 2020
First version publication date	05 December 2020

Trial information

Trial identification

Sponsor protocol code	TEA-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02443935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus N, Denmark, 8200
Public contact	Ole Schmeltz Søgaard, Aarhus University Hospital, 45 78452842, olesoega@rm.dk
Scientific contact	Ole Schmeltz Søgaard, Aarhus University Hospital, 45 78452842, olesoega@rm.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	30 June 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To perform a detailed characterization of the numeric, phenotypic, and functional properties of circulating HIV-1-specific T cells and NK cells during MGN1703 treatment

Protection of trial subjects:

Participants were evaluated by the same physician on each study visit to minimize risk of stress or confusion about procedures and visits. Each participant received a detailed personal overview of scheduled visits. Visits were planned according to participants' wishes regarding time of the day/night, duration etc. Enough time was allowed on each visit for conversation and full clinical evaluation in a non-stressful pace and atmosphere.

Sub-parts of the study (e.g. intestinal biopsy) was optional and not a requirement for enrollment in the main study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2015
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: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited by letter to patients in the Outpatient HIV clinic at the Dept. of Infectious Diseases, Aarhus University Hospital.

Pre-assignment

Screening details:

A total of 18 participants were screened, while 15 met criteria for enrollment. Only participants that met inclusion/exclusion criteria and signed informed consent were enrolled. No participants terminated the study early

Period 1

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

Blinding implementation details:

Study was open-label

Arms

Arm title	Treatment-arm

Arm description:

Study was one-armed, exploratory. Participants received 60 mg investigational medicine twice a week for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Lefitolimod
Investigational medicinal product code	
Other name	MGN1703, dSLIM
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

As 120 mg MGN1703 per week is considered safe in cancer patients and healthy controls, study participants received 4 weeks of 60 mg (concentration 15 mg/mL) of MGN1703, administered subcutaneously by the study investigator as two 2-mL bilateral injections twice weekly. It is injected in either both upper arms, front of the abdomen on each side of the umbilicus or front of the thighs.

Number of subjects in period 1	Treatment-arm
Started	15
Completed	15

Baseline characteristics

Reporting groups

Reporting group title	Study period

Reporting group description: -

Reporting group values	Study period	Total	
Number of subjects	15	15	
Age categorical			
Age defined by visit date minus date of birth			
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)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Not recorded	0	0	
Age continuous			
Units: years			
median	52		
inter-quartile range (Q1-Q3)	46 to 55	-	
Gender categorical			
Gender was defined according to social security number, witch is reflecting the sex of the participant			
Units: Subjects			
Female	2	2	
Male	13	13	
Ethnic group			
Units: Subjects			
White	13	13	
African-danish	2	2	
ART regimen			
Units: Subjects			
PI-based	7	7	
NNRTI-based	6	6	
INI-based Years	2	2	
Age from HIV diagnosis to ART initiation			
Units: Years			
median	0.25		
inter-quartile range (Q1-Q3)	0 to 1.5	-	
Years on ART			
Units: Years			
median	8.6		
inter-quartile range (Q1-Q3)	5.25 to 14.08	-	

Baseline total HIV-1 DNA Units: Copies/million CD4 T cells median inter-quartile range (Q1-Q3)	 400.51 181 to 1010	 -	
Pre ART viral load Units: copies/mL log10 median inter-quartile range (Q1-Q3)	 4.92 2.77 to 5.47	 -	
Years since HIV-1 diagnosis Units: Years median inter-quartile range (Q1-Q3)	 11 5.3 to 15.58	 -	
Nadir CD4+ T-cell count Units: cells/µL median inter-quartile range (Q1-Q3)	 212 29 to 400	 -	

End points

End points reporting groups

Reporting group title	Treatment-arm

Reporting group description:

Study was one-armed, exploratory. Participants received 60 mg investigational medicine twice a week for 4 weeks.

Primary: change in CD69+ expression on NK cells

End point title	change in CD69+ expression on NK cells[1]

End point description:

Statistical analysis was Wilcoxon rank test. Not possible to report in this system as this was a one-armed study

End point type	Primary

End point timeframe:

4 weeks

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 possible to type in statistical analyses as the system does not allow for one-armed study statistical analyses. Please see PMID where statistical analyses were reported

End point values	Treatment-arm			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Percentage	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Increases in plasma interferon alpha

End point title	Increases in plasma interferon alpha

End point description:

End point type	Secondary

End point timeframe:

4 weeks

End point values	Treatment-arm			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: pg/mL				
arithmetic mean (standard deviation)	11.68 (± 14.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in HIV-1 DNA

End point title	Reduction in HIV-1 DNA

End point description:

End point type	Secondary

End point timeframe:

4 weeks

End point values	Treatment-arm			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: copies/million CD4 T cells	124			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

End point title	Safety

End point description:

End point type	Secondary

End point timeframe:

80 days

End point values	Treatment-arm			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Number of adverse events				
number (not applicable)	81			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 80 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4
Reporting groups	
Reporting group title	Treatment-arm
Reporting group description: Study was one-armed, exploratory. Participants received 60 mg investigational medicine twice a week for 4 weeks.	

Serious adverse events	Treatment-arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (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	Treatment-arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 15 (53.33%)		
occurrences (all)	10		
Fever			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Malaise			

subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Injection site reaction			
subjects affected / exposed	9 / 15 (60.00%)		
occurrences (all)	23		
Muscle discomfort			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
insomnia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	10 / 15 (66.67%)		
occurrences (all)	11		
Lymphadenopathy			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Taste disorder			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Gingival bleeding			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
abdominal pain			
subjects affected / exposed	6 / 15 (40.00%)		
occurrences (all)	7		
oral blisters			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Weight loss			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Reduced hair growth			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Upper extremity pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Muscle pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
genital herpes			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 April 2016	Treatment in a "part b" of the trial was included. This part b was extended to 24 weeks

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28329286