EU Clinical Trials Register

Clinical trial results:
Randomized, cohort study of standardized reduction of subcutaneous immunoglobulin treatment in patients with chronic inflammatory demyelinating polyneuropathy

Summary

EudraCT number	2017-002024-24
Trial protocol	DK
Global end of trial date	11 June 2020

Results information

Result version number	v1 (current)
This version publication date	04 December 2021
First version publication date	04 December 2021

Trial information

Trial identification

Sponsor protocol code	AUH-2016-100

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 165, Aarhus N, Denmark, 8200
Public contact	Lars Markvardsen, Aarhus University Hospital, 0045 78450000, larsmark@rm.dk
Scientific contact	Lars Markvardsen, Aarhus University Hospital, 0045 78450000, larsmark@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	31 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To identify the lowest effective dosage of subcutaneous immunoglobulin in maintenance treatment of CIDP

Protection of trial subjects:

All participants had possibility to contact study nurses and physicians during the study period in case of adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 55
Worldwide total number of subjects	55
EEA total number of subjects	55

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)	34
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from outpatient clinics at the neurological departments in Denmark, who are responsible for treatment and follow-up of patients in subcutaneous immunoglobulin for chronic inflammatory demyelinating polyneuropathy (CIDP)

Pre-assignment

Screening details:

Inclusion criteria:
Fulfilling CIDP criteria for propable, possible or definite CIDP (including subtypes)
Stable treament with SCIG (no change in dosage >3 months prior to inclusion)

Screened: n=81
Excluded: n=26; unstable SCIG (n=10), concomittant treatment (n=3), discontinue SCIG (n=2), decline to participate (n=11)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	6 week evaluation

Arm description:

Standardized, tapering off regimen with clinical evaluation every 12th week

Arm type	Experimental
Investigational medicinal product name	Human immunoglobulin for subcutaneous administration
Investigational medicinal product code	
Other name	Gammanorm, Hizentra
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Treatment with SCIG (in percent of individual, pre-study dosage): 90%, 75%, 50%, 25%, 0% (12 weeks treatment for each step)

Arm title	12 week evaluation

Arm description:

Standardized, tapering off regimen with clinical evaluation every 12th week

Arm type	Experimental
Investigational medicinal product name	Human immunoglobulin for subcutaneous administration
Investigational medicinal product code	
Other name	Gammanorm, Hizentra
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Treatment with SCIG (in percent of individual, pre-study dosage): 90%, 75%, 50%, 25%, 0% (12 weeks treatment for each step)

Number of subjects in period 1	6 week evaluation	12 week evaluation
Started	27	28
Completed	11	9
Not completed	16	19
Lack of efficacy	16	19

Baseline characteristics

Reporting groups

Reporting group title	6 week evaluation
Reporting group description:	
Standardized, tapering off regimen with clinical evaluation every 12th week	
Reporting group title	12 week evaluation
Reporting group description:	
Standardized, tapering off regimen with clinical evaluation every 12th week	

Reporting group values	6 week evaluation	12 week evaluation	Total
Number of subjects	27	28	55
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)	19	14	33
From 65-84 years	8	14	22
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	9	7	16
Male	18	21	39

Subject analysis sets

Subject analysis set title	Relapse versus remission
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Analysis of the number of participants dropping out (remission) or excluded (relapse) during stepwise reduction of SCIG dosage indicating active disease	
Subject analysis set title	Frequent versus rare evaluation
Subject analysis set type	Per protocol
Subject analysis set description:	
Evalaution of frequent versus rare clinical evaluation to detect clinical meaningful deterioration	

Reporting group values	Relapse versus remission	Frequent versus rare evaluation	
Number of subjects	55	35	
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)	33	17	
From 65-84 years	22	18	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	6 week evaluation
Reporting group description:	
Standardized, tapering off regimen with clinical evaluation every 12th week	
Reporting group title	12 week evaluation
Reporting group description:	
Standardized, tapering off regimen with clinical evaluation every 12th week	
Subject analysis set title	Relapse versus remission
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Analysis of the number of participants dropping out (remission) or excluded (relapse) during stepwise reduction of SCIG dosage indicating active disease	
Subject analysis set title	Frequent versus rare evaluation
Subject analysis set type	Per protocol
Subject analysis set description:	
Evalaution of frequent versus rare clinical evaluation to detect clinical meaningful deterioration	

Primary: Number of patients in remission

End point title	Number of patients in remission
End point description:	
All patients followed the same dose reduction regimen with the following dosages (pct of SCIG dose at inclusion) Week 0-12: 90% Week 12-24: 75% Week 24-36: 50% Week 36-48: 25% Week 48-60: 0%	
End point type	Primary
End point timeframe:	
From inclusion (week 0) to end-of-study (week 60)	

End point values	6 week evaluation	12 week evaluation	Relapse versus remission	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	27	28	55	
Units: number	11	9	20	

Statistical analyses

Statistical analysis title	Fishers exact test
Comparison groups	6 week evaluation v 12 week evaluation

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.58
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.47

Primary: Total reduction of SCIG dosage

End point title	Total reduction of SCIG dosage

End point description:

All patients followed the same dose reduction regimen with the following dosages (pct of SCIG dose at inclusion)
Week 0-12: 90%
Week 12-24: 75%
Week 24-36: 50%
Week 36-48: 25%
Week 48-60: 0%

End point type	Primary

End point timeframe:

From inclusion (week 0) to end-of-study (week 60)

End point values	6 week evaluation	12 week evaluation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	28		
Units: percent				
median (full range (min-max))	25 (0 to 100)	17.5 (0 to 100)		

Statistical analyses

Statistical analysis title	Overall dosage reduction
Comparison groups	6 week evaluation v 12 week evaluation
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.77
Method	Wilcoxon (Mann-Whitney)

Secondary: Self-registration versus registration at clinic

End point title	Self-registration versus registration at clinic
End point description:	
Number of patients with relapse registered due to a planned clinical evaluation	
End point type	Secondary
End point timeframe:	
From inclusion (week 0) up to end-of-study (week 60)	

End point values	6 week evaluation	12 week evaluation	Frequent versus rare evaluation	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	27	28	35	
Units: numbers	13	11	24	

Statistical analyses

Statistical analysis title	Fisher´s test of relative risk
Statistical analysis description:	
Ability to detect clinical deterioration at clinical visit versus self-registration	
Comparison groups	6 week evaluation v 12 week evaluation
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.17
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.2

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Inclusion (week 0) to end-of-study (week 60)	
Assessment type	Non-systematic

Dictionary used

Dictionary name	Self-reporting
Dictionary version	1

Reporting groups

Reporting group title	Entire cohort
Reporting group description:	
All participants went through the same intervention, only follow regimen was different.	

Serious adverse events	Entire cohort		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Entire cohort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 55 (50.91%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast inflammation			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Nervous system disorders			
Numbness, Muscle fatigue	Additional description: General signs from the nervous system according to the diagnosis CIDP (including numbness, palsies, walking difficulties)		
subjects affected / exposed	6 / 55 (10.91%)		
occurrences (all)	6		
General disorders and administration site conditions			
Dizziness			

subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea, Diarrhoea, Abdominal discomfort			
subjects affected / exposed	8 / 55 (14.55%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	5		
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	2		

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