Clinical trial results:
Measuring effects on pain and quality of life after Dysport® injection in children with cerebral palsy

Summary

EudraCT number	2017-004497-33
Trial protocol	DK
Global end of trial date	31 December 2021

Results information

Result version number	v1 (current)
This version publication date	20 January 2023
First version publication date	20 January 2023
Summary attachment (see zip file)	article (toxins-eudract.docx)

Trial information

Trial identification

Sponsor protocol code	Protocol_Dysport_v3__13.12.2017

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	hvidovre hospital
Sponsor organisation address	keettegaards alle 30, hvidovre, Denmark,
Public contact	Christian Wong, Copenhagen University Hospital at Hvidovre, 0045 38626966, cwon0002@regionh.dk
Scientific contact	Christian Wong, Copenhagen University Hospital at Hvidovre, 0045 38626966, cwon0002@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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2021
Global end of trial reached?	Yes
Global end of trial date	31 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To examine the effect of botulinum toxin injections in regards to pain and quality of life in children with cerebral Palsy

Protection of trial subjects:

following rules of the EC

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2018
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: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	15
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The subjects were paediatric patients with predominantly spastic CP and belonged to all gross motor function classification system (GMFCS) levels. They were recruited from our hospital service area as a convenience sample. Inclusion criteria were children between two and eighteen years of age with spastic cerebral palsy who were botulinum toxin naï

Pre-assignment

Screening details:

Children with CP in our general service area were screened for eligibility. Fifty-one of them had pain and were contacted through their caregivers for inclusion after a formal invitation by letter. After caregivers accepted participation, their medical records were screened according to the inclusion and exclusion criteria. If still eligible, the p

Period 1

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

Blinding implementation details:

No bilinding

Arms

Arm title	followup

Arm description:

Followup to 28 weeks

Arm type	Experimental
Investigational medicinal product name	Dysport
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

A single ultrasound-guided intramuscular injection of AboA was administered without or under general anaesthesia by the discretion of the treating physician. Dosing was determined by the treating physician using 30 units per kilo (U/kg) and 15 U/kg for bilateral and unilateral CP, respectively, with a maximum dose of 1000 units. Small and large muscles were injected within a range of 3–6 U/kg and 8–12 U/kg, respectively. Small muscles were defined as an ultrasound-measured muscle thickness of a ‘diameter’ of less than 0.95 cm at the injection site and large muscles were defined as having a ‘diameter’ larger than 0.95 cm at the injection site [26,27]. Five hundred units of AboA were diluted in 2.5 mL of sterile NaCl in sterile syringes.

Number of subjects in period 1	followup
Started	25
Completed	25

Baseline characteristics

End points

End points reporting groups

Reporting group title	followup

Reporting group description:

Followup to 28 weeks

Subject analysis set title	rflacc score
Subject analysis set type	Full analysis

Subject analysis set description:

2.3. Assessments
The subjects were assessed with observational pain, questionnaires pertaining to pain, function, and quality of life at baseline before injection and after 4, 12, and 28 weeks. Our primary endpoint was the change in pain status from baseline to the initial follow up at four weeks since AboA is considered to have an optimal effect at this time [14]. The subjects were monitored continuously for adverse effects as well as changes in medication or therapeutic interventions.
2.4. Pain Tools
The observational pain tools of the Paediatric pain profile (PPP) and r-FLACC were utilized to captivate different aspects of localized pain. A systematic pain interview was carried out by a single rater.
2.4.1. Localized Muscular Pain Using the Revised Face, Legs Activity, Cry, Consolability Scale
Initial clinical evaluation entailed pROM of all muscles of the lower extremity to identify potential localized muscular pain using the r-FLACC. The r-FLACC scale is a validated behaviou

Primary: rflacc score

End point title	rflacc score

End point description:

Localized Muscular Pain Using the Revised Face, Legs Activity, Cry, Consolability Scale
Initial clinical evaluation entailed pROM of all muscles of the lower extremity to identify potential localized muscular pain using the r-FLACC. The r-FLACC scale is a validated behavioural pain intensity tool with five categories with a three-point ordinal scale (0–2), thus ranging from 0 to 10 possible points. Each category entails a description of behavioural signs in the facial expression, legs, activity, cry and consolability [28]. The r-FLACC scores were evaluated during the examination and were videotaped systematically using two iPads, thus enabling us to re-evaluate the subject in the frontal and sagittal view [29]. The caregivers added a unique descriptive 'pain' behaviour of the child to ensure that our ratings were individual and accurate. The localized pain was evaluated for the treated muscles during the follow ups. Since injections of AboA are presumed to have a localized effect, ou

End point type	Primary

End point timeframe:

after 6 weeks

End point values	followup	rflacc score		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	25[1]	25[2]		
Units: rflacc score				
number (not applicable)				
rflacc	25	25		

Notes:

[1] - all analyzed

[2] - all analyzed

Statistical analyses

Statistical analysis title	Statistical Analysis

Statistical analysis description:

he overall comparisons were between the data at baseline and follow-ups. Shapiro–Wilk for normality was utilized to determine normal distribution. Data from r-FLACC, PPP, and CPCHILD scores were continuous variables and analysed using the paired t-test. Ordinal variables such as impact on activity and SMART goals were not normally distributed and analysed using the Wilcoxon signed-rank test. p-values of ≤0.05 were considered statistically significant. Bonferroni corrections were applied to the r

Comparison groups	followup v rflacc score
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	≥ 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	90 %
sides	2-sided
lower limit	1
upper limit	5
Variability estimate	Standard error of the mean
Dispersion value	2

Notes:

[3] - he overall comparisons were between the data at baseline and follow-ups. Shapiro–Wilk for normality was utilized to determine normal distribution. Data from r-FLACC, PPP, and CPCHILD scores were continuous variables and analysed using the paired t-test. Ordinal variables such as impact on activity and SMART goals were not normally distributed and analysed using the Wilcoxon signed-rank test. p-values of ≤0.05 were considered statistically significant. Bonferroni corrections were applied

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from 2018 to september 2021

Adverse event reporting additional description:

Eleven subjects experienced adverse events during the study. In total, there were sixteen adverse events. The majority were related (12). These were temporary mild (5) and moderate (1) muscle weakness, mild nausea (2), and mild soreness/local bruising (2) at the injection site. Two had moderate pain (2) at the injection site that subsided within th

Assessment type	Non-systematic

Dictionary used

Dictionary name	overnight stay
Dictionary version	1

Reporting groups

Reporting group title	total number

Reporting group description:

Eleven subjects experienced adverse events during the study. In total, there were sixteen adverse events. The majority were related (12). These were temporary mild (5) and moderate (1) muscle weakness, mild nausea (2), and mild soreness/local bruising (2) at the injection site. Two had moderate pain (2) at the injection site that subsided within the first week. An additional three caregivers reported unrelated adverse events with weight gain (1), mild dyspnoea (1), and mild diarrhoea (1) during the study. At the study initiation, one subject (1) had an uneventful admission overnight since the ultrasound-guided injection of AboA was delivered close to an intramuscular vessel. This was classified as a serious adverse event. There was otherwise no expected or unexpected serious adverse events or reactions.

Serious adverse events	total number		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
admission overnight	Additional description: At the study initiation, one subject (1) had an uneventful admission overnight since the ultrasound-guided injection of AboA was delivered close to an intramuscular vessel. This was classified as a serious adverse event.		
subjects affected / exposed	1 / 25 (4.00%)		
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	total number		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 25 (60.00%)		
Product issues			
as described	Additional description: temporary mild (5) and moderate (1) muscle weakness, mild nausea (2), and mild soreness/local bruising (2) at the injection site. Two had moderate pain (2) at the injection site that subsided within the first week.		
subjects affected / exposed[1]	15 / 15 (100.00%)		
occurrences (all)	15		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Eleven subjects experienced adverse events during the study. In total, there were sixteen adverse events. The majority were related (12). These were temporary mild (5) and moderate (1) muscle weakness, mild nausea (2), and mild soreness/local bruising (2) at the injection site. Two had moderate pain (2) at the injection site that subsided within the first week. An additional three caregivers reported unrelated adverse events with weight gain (1), mild dyspnoea (1), and mild diarrhoea (1) during

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35051020