Clinical trial results:
The effect of glycopyrroniumbromide on nocturnal clozapine induced sialorrhea in psychiatric patients: a randomized, cross-over, double blind, placebo controlled trial with an extended open label phase (QUITSPIT study)

Summary

EudraCT number	2012-002299-15
Trial protocol	NL
Global end of trial date	20 June 2015

Results information

Result version number	v1 (current)
This version publication date	05 July 2020
First version publication date	05 July 2020
Summary attachment (see zip file)	Summary (Summary QUITSPIT study.docx)

Trial information

Trial identification

Sponsor protocol code	FIO11-05

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitair Medisch Centrum Utrecht
Sponsor organisation address	Heidelberglaan 100, Utrecht, Netherlands,
Public contact	Ziekenhuisapotheek UMC Utrecht, Universitair Medisch Centrum Utrecht, 0031 887557218, I.Wilting@umcutrecht.nl
Scientific contact	Ziekenhuisapotheek UMC Utrecht, Universitair Medisch Centrum Utrecht, 0031 887557218, I.Wilting@umcutrecht.nl

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	20 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of oral glycopyrroniumbromide in comparison with placebo on the severity of nocturnal sialorrhea in psychiatric patients treated with clozapine

Protection of trial subjects:

Outsome measures were collected during limited amount of visits.
Any possible adverse events were monitored during the weekly patient visits using documentated questionairies

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 September 2012
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	Netherlands: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

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)	32
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Stable users of clozapine using an unchanged clozapine dose for at least 1 month prior to start of the trial. In addition, these subjects were experiencing clozapine induced sialorrhea.

Period 1

Period 1 title	Cross-over 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	No
Arm title	Glycopyrrolate 1mg

Arm description:

Subjects within this arm used glycopyrrolate 1mg/day during 6 days

Arm type	Experimental
Investigational medicinal product name	Glycopyrrolate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Subjects within this arm used glycopyrrolate 1mg/day using 0.2mg/ml oral solution during 6 days

Arm title	Placebo

Arm description:

Subjects within this arm used placebo during 6 days

Arm type	Placebo
Investigational medicinal product name	Placebo solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects within this arm used 5 ml of the placebo solution during 6 days

Number of subjects in period 1	Glycopyrrolate 1mg	Placebo
Started	16	16
Completed	16	16

Period 2	
Period 2 title	Wash-out 1
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Arm title	Wash-out
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Wash-out
Started	32
Completed	32

Period 3	
Period 3 title	Cross-over 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor
Arms	
Are arms mutually exclusive?	Yes
Arm title	Glycopyrrolate 1mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Glycopyrrolate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Subjects within this arm used glycopyrrolate 1mg/day using 0.2mg/ml oral solution during 6 days

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Subjects within this arm used 5 ml of the placebo solution during 6 days

Number of subjects in period 3	Glycopyrrolate 1mg	Placebo
Started	16	16
Completed	16	16

Period 4	
Period 4 title	Wash-out 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Wash out
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 4	Wash out
Started	32
Completed	23
Not completed	9
Lost to follow-up	9

Period 5	
Period 5 title	Open label
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Arm title	Glycopyrrolate 2mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Glycopyrrolate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

During the open label phase, subject used 2 mg glycopyrrolate/day during 6 days

Number of subjects in period 5	Glycopyrrolate 2mg
Started	23
Completed	23

Baseline characteristics

Reporting groups	
Reporting group title	Cross-over 1

Reporting group description: -

Reporting group values	Cross-over 1	Total	
Number of subjects	32	32	
Age categorical Units: Subjects			
Adults (18-65 years)	32	32	
Gender categorical Units: Subjects			
Female	11	11	
Male	21	21	

End points

End points reporting groups

Reporting group title	Glycopyrrolate 1mg
Reporting group description: Subjects within this arm used glycopyrrolate 1mg/day during 6 days	
Reporting group title	Placebo
Reporting group description: Subjects within this arm used placebo during 6 days	
Reporting group title	Wash-out
Reporting group description: -	
Reporting group title	Glycopyrrolate 1mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Wash out
Reporting group description: -	
Reporting group title	Glycopyrrolate 2mg
Reporting group description: -	

Primary: Clinical improvement of CIS assessed by the Patient Global Impression of Improvement (PGI-I)

End point title	Clinical improvement of CIS assessed by the Patient Global Impression of Improvement (PGI-I)
End point description:	
End point type	Primary
End point timeframe: Assesments for the end point were performed after period 3 'cross-over 2' and after period 5 'open label'	

End point values	Glycopyrrolate 1mg	Placebo	Glycopyrrolate 1mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	16	16
Units: Percentage	0	4	2	2

End point values	Glycopyrrolate 2mg			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Percentage	10			

Statistical analyses

Statistical analysis title	McNemar’s test
Comparison groups	Placebo v Glycopyrrolate 1mg v Glycopyrrolate 1mg v Placebo v Glycopyrrolate 2mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mcnemar
Parameter estimate	Risk ratio (RR)
Point estimate	6.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	20.36

Adverse events

Adverse events information	
Timeframe for reporting adverse events: adverse events assesments were performed after each period	
Adverse event reporting additional description: Adverse events of glycopyrrolate, in terms of worsening of baseline events were assessed	
Assessment type	Systematic

Dictionary used	
Dictionary name	other
Dictionary version	1

Reporting groups	
Reporting group title	Glycopyrrolate 1mg
Reporting group description: Subjects within this arm used glycopyrrolate 1mg/day during 6 days	
Reporting group title	Placebo
Reporting group description: Subjects within this arm used placebo during 6 days	

Serious adverse events	Glycopyrrolate 1mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Glycopyrrolate 1mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 32 (15.63%)	5 / 32 (15.63%)	
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	3 / 32 (9.38%)	2 / 32 (6.25%)	
occurrences (all)	3	2	
Nervous system disorders			
Shortened sleep			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	
occurrences (all)	2	1	
General disorders and administration site conditions			

Headache subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	2 / 32 (6.25%) 2	
Social circumstances Nervousness subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1	2 / 32 (6.25%) 2	
Endocrine disorders Diaphoresis subjects affected / exposed occurrences (all)	3 / 32 (9.38%) 3	2 / 32 (6.25%) 2	
Metabolism and nutrition disorders Xerostomia subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2	2 / 32 (6.25%) 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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28129312