Clinical trial results:
Ensayo clínico piloto, aleatorizado, controlado con placebo, paralelo, para evaluar la eficacia y seguridad de la tobramicina inhalada, en el paciente afecto de bronquiectasias, sin fibrosis quística e infección bronquial intermitente por Pseudomonas aeruginosa.

Summary

EudraCT number	2005-005820-15
Trial protocol	ES
Global end of trial date	31 December 2013

Results information

Result version number	v1 (current)
This version publication date	13 November 2021
First version publication date	13 November 2021

Trial information

Trial identification

Sponsor protocol code	ORRI-4

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, VHIR, joaquin.lopez.soriano@vhir.org
Scientific contact	Ramon Orriols, VHIR, raorriols.girona.ics@gencat.cat

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 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determinar si ell uso de tobramicina inhalada en los sujetos afectos de bronquiectasias e infección inicial o intermitente por Pseudomonas aeruginosa evita o retrasa la aparición de un nuevo cultivo positivo a Pseudomonas aeruginosa y aumenta el tiempo libre de exacerbaciones secundarias a Pseudomonas aeruginosa.
To evaluate the efficacy of 3 months of nebulised tobramycin after a short course of intravenous antibiotics in the eradication of P. aeruginosa and its clinical consequences in nonCF bronchiectasis following initial P. aeruginosa infection.

Protection of trial subjects:

During the 3 first months, all patients were controlled monthly and 5, 7, 9, 12 and 15 months thereafter. The number of exacerbations, number of hospital admissions and days of hospitalisation were registered. Supplementary use of oral antibiotics was allowed on the development of an exacerbation, defined as more frequent coughing, greater dyspnoea and an increase in sputum volume and purulence

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2006
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	Spain: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

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)	0
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	35
Number of subjects completed	35

Period 1

Period 1 title	Tobramycin (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Tobramycin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tobramycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

300 mg twice daily for 3 months, nebulized solution for inhalatiom

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Twice daily during 3 motnhs, volumes equivalent to experimental group

Number of subjects in period 1	Tobramycin	Placebo
Started	16	19
Completed	11	17
Not completed	5	2
Physician decision	5	-
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Tobramycin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Tobramycin	Placebo	Total
Number of subjects	16	19	35
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	69.4	70.11	
standard deviation	± 2.1	± 1.9	-
Gender categorical Units: Subjects			
Female	6	10	16
Male	10	9	19

End points

End points reporting groups	
Reporting group title	Tobramycin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Ps aeruginosa in sputum	
End point title	Ps aeruginosa in sputum
End point description:	
End point type	Primary
End point timeframe:	
End of study (15 months)	

End point values	Tobramycin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	17		
Units: percent				
number (not applicable)	54.5	29.4		

Statistical analyses

Statistical analysis title	P aeruginosa in sputum
Comparison groups	Tobramycin v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.048
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 15 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	Total adverse events

Reporting group description: -

Serious adverse events	Total adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (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	Total adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 35 (14.29%)		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	5		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Nebulised tobramycin therapy had to be discontinued due to bronchospasm in 5 patients, suggesting that the risk of this complication should be considered in patients with low FEV1 values. Larger number of patients and longer follow-up are desired

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26340658