Clinical trial results:
A PROSPECTIVE, RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF PRE-TRANSPLANT AND PROMPT POST-TRANSPLANT TREATMENT WITH AZITHROMYCIN TO IMPROVE EARLY ALLOGRAFT FUNCTION AND OUTCOME AFTER LUNG TRANSPLANTATION

Summary

EudraCT number	2012-003331-32
Trial protocol	BE
Global end of trial date	07 April 2018

Results information

Result version number	v1 (current)
This version publication date	16 December 2020
First version publication date	16 December 2020
Summary attachment (see zip file)	Final results AZI0003 (Results AZI003 paper Vos.pdf)

Trial information

Trial identification

Sponsor protocol code	AZI003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01915082
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	KU Leuven
Sponsor organisation address	49 Herestraat , Leuven, Belgium, B-3000
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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	08 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 April 2018
Global end of trial reached?	Yes
Global end of trial date	07 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Improvement in mean pulmonary function (FEV1; %pred) during the first 3 months after lung transplantation

Protection of trial subjects:

Routine post-transplant follow-up, immunosuppressive regimen and infectious prophylaxis was given to all patients according to standardized protocols, independent of study drug.
Adverse events were monitored by the treating LTx clinician (blinded for study-drug) and were defined as hearing loss, cardiac arrhythmias (e.g. torsade de pointes), serious allergic reactions including skin reactions (rash, urticaria or Stevens-Johnson syndrome), angioneurotic edema and anaphylaxis and neurologic disorders (convulsions).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 2013
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	Belgium: 68
Worldwide total number of subjects	68
EEA total number of subjects	68

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)	68
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

120 patients who underwent double LTx between October 2013 and October 2015 were screened for inclusion.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Azithromycin

Arm description:

Study drug was added to standard of care and was administered once immediately before LTx (1000 mg of azithromycin or placebo) and every other day from day 1 until day 31 after LTx (250 mg of azithromycin or placebo).

Arm type	Experimental
Investigational medicinal product name	azithromycin
Investigational medicinal product code	
Other name	Zitromax® oral suspension 200 mg/ 5 mL
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Zitromax® oral suspension 200 mg/ 5 mL

Arm title	PLacebo

Arm description:

Ora-plus (97% purified water, <1% Sodium phosphate monobasic, <1% Sodium carboxymethylcellulose, <1% Microcrystalline cellulose, <1% Xanthan gum, <1% Carrageenan)

Arm type	Placebo
Investigational medicinal product name	Ora-plus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Ora-plus (97% purified water, <1% Sodium phosphate monobasic, <1% Sodium carboxymethylcellulose, <1% Microcrystalline cellulose, <1% Xanthan gum, <1% Carrageenan) suspension

Number of subjects in period 1	Azithromycin	PLacebo
Started	34	34
Completed	34	34

Baseline characteristics

End points

End points reporting groups

Reporting group title	Azithromycin
Reporting group description:	
Study drug was added to standard of care and was administered once immediately before LTx (1000 mg of azithromycin or placebo) and every other day from day 1 until day 31 after LTx (250 mg of azithromycin or placebo).	
Reporting group title	PLacebo
Reporting group description:	
Ora-plus (97% purified water, <1% Sodium phosphate monobasic, <1% Sodium carboxymethylcellulose, <1% Microcrystalline cellulose, <1% Xanthan gum, <1% Carrageenan)	

Primary: Pulmonary function

End point title	Pulmonary function
End point description:	
End point type	Primary
End point timeframe:	
3 months after transplant	

End point values	Azithromycin	PLacebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	34		
Units: percentage predicted				
median (inter-quartile range (Q1-Q3))	5 (1 to 10)	6 (2 to 11)		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Patient proportions were compared using the chi-squaretest. Continuous data are presented as mean and standard error ofthe mean when normally distributed, or as a median with inter-quartile range when non–normally distributed. Group means werecompared using unpaired, two-tailedt-test or Mann–WhitneyU-test for normally or non–normally distributed variables, respectively. GraphPad Prism 6.0 software (GraphPad) was used for statistical analysis. p-values are two-sided, with $p<0.05$ significant.	
Comparison groups	Azithromycin v PLacebo
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

At every patient contact during the study period, minimum at least every 4 months

Adverse event reporting additional description:

None of the previously defined adverse events were reported in either the study or placebo group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	placebo

Reporting group description: -

Reporting group title	azithromycin

Reporting group description: -

Serious adverse events	placebo	azithromycin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	
number of deaths (all causes)	6	4	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	placebo	azithromycin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No predefined adverse events were recorded

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/30686699