

**Clinical trial results:****Efficacy of Pidotimod in the prevention of respiratory infections in healthy children: a randomized, double blind, placebo controlled study.****Summary**

EudraCT number	2013-002273-22
Trial protocol	IT
Global end of trial date	25 November 2014

Results information

Result version number	v1 (current)
This version publication date	19 March 2020
First version publication date	19 March 2020

Trial information**Trial identification**

Sponsor protocol code	1/2013
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Azienda Ospedaliera L. Sacco, Clinica Pediatrica
Sponsor organisation address	Via Giovanni Battista Grassi, 74, Milano, Italy, 20157
Public contact	Clinica Pediatrica, Azienda Ospedaliera L. Sacco, 0039 0239042253, gianvincenzo.zuccotti@unimi.it
Scientific contact	Clinica Pediatrica, Azienda Ospedaliera L. Sacco, 0039 0239042253, gianvincenzo.zuccotti@unimi.it

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	25 November 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of Pidotimod in reducing the rate of respiratory infections in healthy children.

Protection of trial subjects:

No specific measures were put in place to protect the subjects enrolled in the trial. Patients' parents could withdraw at any time during the study either spontaneously or on indication of the paediatrician.

Background therapy:

None

Evidence for comparator:

None

Actual start date of recruitment	20 September 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	Italy: 57
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	57
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From 1 to 19 October 2013 children were recruited by a sample of 17 family pediatricians working for the Italian National Health System in Milan and Vicenza (Italy). A total of 800 children were evaluated for potential enrollment; 733 subjects did not meet the inclusion criteria and 10 refused to participate.

Pre-assignment

Screening details:

Healthy children of both sexes in the 4th year of life at the time of recruitment, Caucasian, registered with the Azienda Sanitaria Locale with a family paediatrician involved in the study, who had never attended the nursery school were considered in the study.

Period 1

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

Blinding implementation details:

Pidotimod and placebo pills were of the same number, size, appearance and taste. Blindness of patients and pediatricians was ensured by using packages that reported only the progressive number of the subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pidotimod

Arm description:

Pidotimod

Arm type	Experimental
Investigational medicinal product name	pidotimod
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

400 mg twice at day for the last 10 days of each month from October 2013 to April 2014

Arm title	Placebo
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Arm description:

Placebo

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

Dosage and administration details:

400 mg twice at day for the last 10 days of each month from October 2013 to April 2014.

Number of subjects in period 1	Pidotimod	Placebo
Started	29	28
Completed	24	25
Not completed	5	3
Lost to follow-up	5	3

Baseline characteristics

Reporting groups

Reporting group title	Pidotimod
Reporting group description: Pidotimod	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	Pidotimod	Placebo	Total
Number of subjects	29	28	57
Age categorical			
Units: Subjects			
Children (2-11 years)	29	28	57
Age continuous			
Units: years			
arithmetic mean	3.3	3.3	
standard deviation	± 0.3	± 0.3	-
Gender categorical			
Units: Subjects			
Female	9	12	21
Male	20	16	36
Gestational age			
Units: Subjects			
Not available	0	1	1
>37 weeks	20	23	43
<37 weeks	4	1	5
Lost to follow-up	5	3	8
Immunization with hesavalent vaccine			
Units: Subjects			
Yes	24	25	49
No	0	0	0
Lost to follow-up	5	3	8
Immunization with pneumococcal 13-valent vaccine			
Units: Subjects			
Yes	20	22	42
No	4	3	7
Lost to follow-up	5	3	8
Previous hospitalization for a respiratory infection			
Units: Subjects			
Yes	3	1	4
No	21	24	45
Lost to follow-up	5	3	8

End points

End points reporting groups

Reporting group title	Pidotimod
Reporting group description:	Pidotimod
Reporting group title	Placebo
Reporting group description:	Placebo

Primary: Infection rate

End point title	Infection rate
End point description:	
End point type	Primary
End point timeframe:	From September 2013 to March 2014

End point values	Pidotimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Infection rate				
number (confidence interval 95%)	1.9 (1.3 to 2.4)	2.4 (1.8 to 3.0)		

Statistical analyses

Statistical analysis title	Infection Rate Ratio
Statistical analysis description:	Poisson regression model having the number of infections developed during the study as response variable and the treatment group (0 = placebo; 1 = Pidotimod) as predictor.
Comparison groups	Pidotimod v Placebo
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.211
Method	Poisson
Parameter estimate	Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.15

Secondary: Antibiotics Prescription Rate

End point title	Antibiotics Prescription Rate
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End point description:

End point type	Secondary
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End point timeframe:

From September 2013 to March 2014

End point values	Pidotimod	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Prescription				
number (confidence interval 95%)	0.29 (0.11 to 0.47)	0.52 (0.32 to 0.72)		

Statistical analyses

Statistical analysis title	Risk ratio for antibiotic prescription
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Statistical analysis description:

Binomial regression model having the use of antibiotics at any time during the study (0 = no; 1 = yes) as response variable and the treatment group (0 = placebo; 1 = Pidotimod) as predictor.

Comparison groups	Pidotimod v Placebo
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Number of subjects included in analysis	49
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Analysis specification	Pre-specified
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Analysis type	other
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P-value	= 0.12
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Method	Binomial regression
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Parameter estimate	Risk ratio (RR)
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Point estimate	0.56
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	0.27
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upper limit	1.16
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Adverse events

Adverse events information

Timeframe for reporting adverse events:

From September 2013 to March 2014

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Overall population
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Reporting group description: -

Serious adverse events	Overall population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 57 (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	Overall population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 57 (1.75%)		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		

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.

Neither limitations or caveats are applicable to this summary of the results
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Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25931316>