



Clinical trial results:

Efficacy and tolerability clinical trial of Lantigen B (A bacterial lysate having immunostimulating activity) in the prophylaxis of respiratory infections, with special reference to patients with allergy to perennial inhalants. Double-blind multicenter, randomized study vs. placebo.

Summary

EudraCT number	2011-003239-76
Trial protocol	IT
Global end of trial date	28 October 2013

Results information

Result version number	v1 (current)
This version publication date	21 February 2020
First version publication date	21 February 2020

Trial information

Trial identification

Sponsor protocol code	LAN-BR-11-001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bruschettini S.r.l.
Sponsor organisation address	Via Isonzo, Genoa, Italy, 16127
Public contact	Clinical Research Department, Medi Service SRL, 0039 039-6057074, medi@mediservice.it
Scientific contact	Clinical Research Department, Medi Service SRL, 0039 039-6057074, medi@mediservice.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	10 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 October 2013
Global end of trial reached?	Yes
Global end of trial date	28 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy of LANTIGEN B vs. placebo, in reducing, during a 8-month period, the number of infective episodes of the respiratory tract .

Protection of trial subjects:

During the study follow-up, to minimise the patients pain/distress, it was permitted to take the following concomitant medications:

antibiotics, decongestant, mucolytics.

Background therapy:

During the two weeks preceding the randomization the following drugs were not allowed: Immune-stimulants, gamma-globulines, etc. of the ATC group J06 and J07AX; Anti-neoplastic drugs of the ATC group L01; Cytokines, interleukins, interferon, immune-suppressants of the ATC group L03 and L04.

After the randomization and during the study (including the follow-up period) the following drugs were not permitted: Immune-stimulants of the ATC group J07AX; Anti-neoplastic drugs of the ATC group L01; Cytokines, interleukins, interferon, immune-suppressants of the ATC group L03 and L04; Systemic steroids (if used for more than 2 weeks); Any drug product or dietary supplement containing zinc (if used for more than one week); Any other product with immune-stimulant features.

Evidence for comparator: -

Actual start date of recruitment	03 September 2012
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: 160
Worldwide total number of subjects	160
EEA total number of subjects	160

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)	151
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 160 subjects were enrolled in 12 Italian Clinical Centres in the period September 2012 - January 2013.

Pre-assignment

Screening details:

Run-in and/or screening periods were not planned in the study design. Randomization visit (Visit 1) was considered as baseline period.

Wash-out period: during the two weeks preceding the randomization the following drugs were not allowed: ATC groups J06, J07AX, L01, L03 and L04.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Lantigen B

Arm description:

Lantigen B is a suspension of bacterial antigens obtained from Streptococcus pneumoniae type 3, Streptococcus pyogenes Group A, Branhamella catarrhalis, Staphylococcus aureus, Hemophilus influenzae type b and Klebsiella pneumoniae.

Arm type	Experimental
Investigational medicinal product name	Lantigen B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Administration: 15 oral drops twice daily (morning and evening) for 4 weeks, followed by 2 weeks off + 4 weeks of treatment + 6 weeks off, for a total of 16 weeks in two cycles.

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	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Administration: 15 oral drops twice daily (morning and evening) for 4 weeks, followed by 2 weeks off + 4 weeks of treatment + 6 weeks off, for a total of 16 weeks in two cycles

Number of subjects in period 1	Lantigen B	placebo
Started	79	81
Completed	62	58
Not completed	17	23
Familiar reasons	-	1
Consent withdrawn by subject	10	13
Adverse event, non-fatal	1	2
Patient not contactable	-	1
Lost to follow-up	1	4
Protocol deviation	5	2

Baseline characteristics

Reporting groups

Reporting group title	Lantigen B
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Reporting group description:

Lantigen B is a suspension of bacterial antigens obtained from *Streptococcus pneumoniae* type 3, *Streptococcus pyogenes* Group A, *Branhamella catarrhalis*, *Staphylococcus aureus*, *Hemophilus influenzae* type b and *Klebsiella pneumoniae*.

Reporting group title	placebo
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Reporting group description:

placebo

Reporting group values	Lantigen B	placebo	Total
Number of subjects	79	81	160
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			
arithmetic mean	42.38	42.43	
standard deviation	± 13.937	± 15.146	-
Gender categorical			
Units: Subjects			
Female	54	58	112
Male	25	23	48
Number of previous infectious episodes			
Number of infectious episodes of the respiratory tract in the previous year.			
Units: number			
arithmetic mean	3.67	3.84	
standard deviation	± 1.615	± 1.337	-
Number of previous allergic episodes			
Number of allergic episodes in the previous year.			
Units: number			
arithmetic mean	1.57	1.25	
standard deviation	± 4.376	± 2.467	-

End points

End points reporting groups

Reporting group title	Lantigen B
Reporting group description: Lantigen B is a suspension of bacterial antigens obtained from Streptococcus pneumoniae type 3, Streptococcus pyogenes Group A, Branhamella catarrhalis, Staphylococcus aureus, Hemophilus influenzae type b and Klebsiella pneumoniae.	
Reporting group title	placebo
Reporting group description: placebo	

Primary: Number of respiratory infectious episode

End point title	Number of respiratory infectious episode
End point description: An infectious episode was defined as "new" if at least 72 hours had passed, in the complete absence of symptoms, from the resolution of the previous episode.	
End point type	Primary
End point timeframe: Respiratory infectious episodes during the 8 months of follow-up	

End point values	Lantigen B	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 ^[1]	58 ^[2]		
Units: number				
arithmetic mean (standard deviation)	0.86 (± 1.238)	1.43 (± 1.613)		

Notes:

[1] - ITT Population

[2] - ITT population

Statistical analyses

Statistical analysis title	Independent-Samples t-test / GLM analysis
Statistical analysis description: Independent-Samples t-test. ANCOVA Analysis, adjusting for the number of previous infectious episodes and gender.	
Comparison groups	Lantigen B v placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.036 ^[4]
Method	t-test, 2-sided
Parameter estimate	Cox proportional hazard

Notes:

[3] - ITT Population: Primary end-point analysis

[4] - ANCOVA, applied by adjusting for the number of previous infectious episodes and gender, confirmed this finding (p=0.019).
Wilcoxon Rank-sum Test p-value = 0.080.

Secondary: Number of days with respiratory infectious episodes

End point title	Number of days with respiratory infectious episodes
End point description:	
Number of days with respiratory infectious episodes during 8 months	
End point type	Secondary
End point timeframe:	
8 months follow-up study	

End point values	Lantigen B	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 ^[5]	58 ^[6]		
Units: number				
arithmetic mean (standard deviation)	5.83 (± 9.839)	10.14 (± 15.575)		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

Statistical analysis title	Independent-Samples t-test / GLM analysis
Statistical analysis description:	
Independent-Samples t-test.	
ANCOVA Analysis, adjusting for the number of previous infectious episodes and gender.	
Comparison groups	Lantigen B v placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	= 0.076 ^[8]
Method	t-test, 2-sided

Notes:

[7] - Secondary end-point analysis.

[8] - The ANCOVA, applied by adjusting for the number of previous infectious episodes and gender, confirmed this finding (p=0.102).

Secondary: Number of days with episodes of allergy

End point title	Number of days with episodes of allergy
End point description:	
Number of days with episodes of allergy during the 8 months of follow-up.	
End point type	Secondary
End point timeframe:	
During the 8 months of follow-up study.	

End point values	Lantigen B	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 ^[9]	58 ^[10]		
Units: Number				
arithmetic mean (standard deviation)	12.69 (± 31.701)	2.84 (± 7.991)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

Statistical analysis title	Independent-Samples t-test / GLM analysis
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Statistical analysis description:

Independent-Samples t-test.

ANCOVA Analysis, adjusting for the number of previous infectious episodes and gender.

Comparison groups	Lantigen B v placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority ^[11]
P-value	= 0.024 ^[12]
Method	t-test, 2-sided

Notes:

[11] - Secondary end-point analysis

[12] - The ANCOVA, applied by adjusting for the number of previous infectious episodes and gender, not confirmed this finding (p=0.056).

Secondary: Number of days lost at work or school

End point title	Number of days lost at work or school
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End point description:

End point type	Secondary
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End point timeframe:

Period: 8 months follow-up study.

End point values	Lantigen B	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 ^[13]	57 ^[14]		
Units: number				
arithmetic mean (standard deviation)	0.75 (± 2.570)	0.79 (± 2.433)		

Notes:

[13] - ITT Population

[14] - ITT Population (missing value for 1 subject)

Statistical analyses

Statistical analysis title	Independent-Samples t-test
Comparison groups	Lantigen B v placebo

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority ^[15]
P-value	= 0.925
Method	t-test, 2-sided

Notes:

[15] - Secondary end-point analysis

Secondary: General well-being

End point title	General well-being
End point description:	
Evaluated by the subjects using a VAS scale (from 0 to 10).	
End point type	Secondary
End point timeframe:	
End of Study: after 2 treatment cycles.	

End point values	Lantigen B	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 ^[16]	56 ^[17]		
Units: number				
arithmetic mean (standard deviation)	7.28 (± 1.708)	7.47 (± 1.283)		

Notes:

[16] - ITT population

[17] - ITT population: missing values for 2 subjects.

Statistical analyses

Statistical analysis title	Independent-Samples t-test
Comparison groups	Lantigen B v placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority ^[18]
P-value	= 0.496
Method	t-test, 2-sided

Notes:

[18] - Secondary end-point analysis

Secondary: Global efficacy

End point title	Global efficacy
End point description:	
The global efficacy was evaluated by the Investigator using a 5-item scale.	
End point type	Secondary
End point timeframe:	
End of Study Visit	

End point values	Lantigen B	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58 ^[19]	57 ^[20]		
Units: number				
Worsened	2	3		
Unchanged	25	22		
Improved	31	32		

Notes:

[19] - ITT Population: missing value for 1 subject

[20] - ITT Population: missing value for 1 subject

Statistical analyses

Statistical analysis title	Chi Square test
Comparison groups	Lantigen B v placebo
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority ^[21]
P-value	= 0.686
Method	Chi-squared

Notes:

[21] - Secondary end-point analysis

Secondary: Global safety

End point title	Global safety
End point description:	
The global safety was evaluated by the Investigator using a 5-item scale.	
End point type	Secondary
End point timeframe:	
End of Study Visit	

End point values	Lantigen B	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 ^[22]	57 ^[23]		
Units: number				
Excellent	24	21		
Good	30	29		
Fair	5	7		

Notes:

[22] - ITT Population

[23] - ITT Population: missing value for 1 subject

Statistical analyses

Statistical analysis title	Chi Square test
Comparison groups	Lantigen B v placebo

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.735
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events reported during the study (from baseline to the last visit) were taken into account.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Lantigen B
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Reporting group description:

Lantigen B is a suspension of bacterial antigens obtained from Streptococcus pneumoniae type 3, Streptococcus pyogenes Group A, Branhamella catarrhalis, Staphylococcus aureus, Hemophilus influenzae type b and Klebsiella pneumoniae.

Reporting group title	placebo
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Reporting group description:

placebo

Serious adverse events	Lantigen B	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 76 (2.63%)	1 / 74 (1.35%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung Cancer			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Nasopharynx biopsy			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hip prosthesis insertion			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	Lantigen B	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 76 (13.16%)	15 / 74 (20.27%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Cryosurgery of turbinates			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 76 (2.63%)	0 / 74 (0.00%)	
occurrences (all)	2	0	
Migraine			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 76 (0.00%)	2 / 74 (2.70%)	
occurrences (all)	0	2	
Social circumstances			
Premenopause			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	2	
Nausea			

subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Duodenogastric reflux			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Tooth abscess			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 76 (1.32%)	2 / 74 (2.70%)	
occurrences (all)	2	3	
Chest pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
skin rash			
subjects affected / exposed	0 / 76 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Renal and urinary disorders			

Genitourinary tract infection subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 2	0 / 74 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 3	1 / 74 (1.35%) 1	
Arthralgia subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 74 (0.00%) 0	
Pain ankle subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	0 / 74 (0.00%) 0	
Lipoma subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 74 (1.35%) 1	
Infections and infestations			
Candida infection subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 2	1 / 74 (1.35%) 1	
Herpes labialis subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 74 (1.35%) 1	
Metabolism and nutrition disorders			
Hypothyroidism subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	1 / 74 (1.35%) 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

None reported