Clinical trial results:
Blood glucose control with BioChaperone insulin lispro compared to insulin lispro (Humalog®) after ingestion of a standardised meal.

Summary

EudraCT number	2014-005028-92
Trial protocol	DE
Global end of trial date	13 March 2015

Results information

Result version number	v1 (current)
This version publication date	16 September 2020
First version publication date	16 September 2020

Trial information

Trial identification

Sponsor protocol code	BC3-CT011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02344992
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Adocia
Sponsor organisation address	115 Avenue Lacassagne, LYON, France, 69003
Public contact	Deputy General Manager, Adocia, +33 472610610, o.soula@adocia.com
Scientific contact	Director of Clinical Development, Adocia, +33 472610610, g.meiffren@adocia.com

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	11 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Comparison of postprandial blood glucose (BG) control after administration of BioChaperone insulin lispro (BC Lispro) and Humalog® at the start (t=0) of a standardised meal ingestion.

Protection of trial subjects:

The trial was conducted in accordance with the declaration of Helsinki and International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceutical use (ICH) Good Clinical Practices.

Background therapy:

I

Evidence for comparator: -

Actual start date of recruitment	14 January 2015
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	Germany: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	38
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at one site in Germany

Pre-assignment

Screening details:

MAle or Female subjects aged from 18 to 64 years with type 1 diabetes mellitus for at least 1 year.
HbA1C% equal or less than 9.0%
BMI between 18.5 and 28.0 kg/m²

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	Subject, Investigator, Monitor

Blinding implementation details:

An authorised unblinded person prepared and administered the trial drug according to the randomisation based assignment to one of the predefined treatment sequences. Except for the unblinded persons involved in the preparation & administration of the trial drug (persons not involved in any other clinical trial activities), everyone in the trial inclusive the PK laboratory was blinded until after completion of the trial and the final data review.

Arms

Arm title	BC Lispro / Humalog®

Arm description:

Each subject was randomly allocated to a sequence of two treatments applied at two separate dosing visits, i.e. with one single dose (0.2U·kg-1BW) of Humalog® injected immediately prior to the start of meal ingestion (0 minutes), or a single dose (0.2U·kg-1BW) of BC Lispro injected immediately prior to the start of meal ingestion (0 minutes).
Subjects stayed at the clinical trial centre until the 8-hour standardised test-meal procedure was terminated. The two dosing visits will be separated by a wash-out period of 3-15 days.

Arm type	Cross-over (experimental & active comparator)
Investigational medicinal product name	Biochaperone insulin lispro
Investigational medicinal product code	
Other name	BC lispro
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A single dose of 0.2 U/kg body weight was administered subcutaneously with a disposable syringe.

Investigational medicinal product name	Humalog®
Investigational medicinal product code	
Other name	Insulin lispro
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A single dose of 0.2 U/kg body weight was administered subcutaneously with a disposable syringe.

Number of subjects in period 1	BC Lispro / Humalog®
Started	38
Completed	38

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	38	38	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	38	38	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	35	35	

Subject analysis sets	
Subject analysis set title	BC Lispro
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received at least one dose of BC Lispro

Subject analysis set title	Humalog®
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received at least one dose of Humalog®

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjeects who received at least one dose of IMP (study drug)

Reporting group values	BC Lispro	Humalog®	Safety population
Number of subjects	38	38	38
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	38	38	38
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	3	3	3
Male	35	35	35

End points

End points reporting groups

Reporting group title	BC Lispro / Humalog®
Reporting group description:	
Each subject was randomly allocated to a sequence of two treatments applied at two separate dosing visits, i.e. with one single dose (0.2U·kg-1BW) of Humalog® injected immediately prior to the start of meal ingestion (0 minutes), or a single dose (0.2U·kg-1BW) of BC Lispro injected immediately prior to the start of meal ingestion (0 minutes). Subjects stayed at the clinical trial centre until the 8-hour standardised test-meal procedure was terminated. The two dosing visits will be separated by a wash-out period of 3-15 days.	
Subject analysis set title	BC Lispro
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who received at least one dose of BC Lispro	
Subject analysis set title	Humalog®
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who received at least one dose of Humalog®	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjeects who received at least one dose of IMP (study drug)	

Primary: ΔAUCBG,0-2h

End point title	ΔAUCBG,0-2h
End point description:	
Area under the blood glucose concentration-time curve from 0-2 hours after a standardised liquid meal	
End point type	Primary
End point timeframe:	
From t=0 to t=2 hour after the standardised liquid meal	

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: mg.h/dL				
arithmetic mean (standard deviation)	54.402 (± 56.981)	109.97 (± 62.498)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	Humalog® v BC Lispro

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.284
upper limit	0.524

Notes:

[1] - Differences

Secondary: BG1h

End point title	BG1h

End point description:

Blood glucose concentration at 1 hour after a standardised liquid meal.

End point type	Secondary

End point timeframe:

From t=0 to t=1h after the standardised liquid meal.

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: mg/dL				
arithmetic mean (standard deviation)	135.2 (± 37.30)	176.7 (± 40.09)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.692
upper limit	0.831

Notes:
[2] - Differences

Secondary: BG2h

End point title	BG2h
End point description:	
blood glucose concentration at 2 hours after a standardised meal	
End point type	Secondary
End point timeframe:	
From t=0 to t=2h after the standardised meal	

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: mg/dL				
arithmetic mean (standard deviation)	126.1 (± 48.13)	153.3 (± 55.72)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.0006
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.737
upper limit	0.913

Notes:
[3] - Differences

Secondary: AUCIns(0-30min)

End point title	AUCIns(0-30min)
End point description:	
Area under the serum insulin lispro concentration-time curve from 0-30 min	
End point type	Secondary
End point timeframe:	
From t=0 to t=30min after dosing	

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: h.mU/L				
arithmetic mean (standard deviation)	25.190 (± 11.026)	10.629 (± 5.5779)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.18
upper limit	3.303

Notes:

[4] - Differences

Secondary: AUCins(0-1h)

End point title	AUCins(0-1h)
End point description:	
Area under the serum insulin lispro concentration-time curve from 0-1 hour	
End point type	Secondary
End point timeframe:	
From T=0 to t=1h after dosing	

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: h.mU/L				
arithmetic mean (standard deviation)	81.430 (± 32.224)	55.179 (± 22.125)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	Humalog® v BC Lispro
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.371
upper limit	1.675

Notes:
[5] - Differences

Secondary: AUCins(0-8h)

End point title	AUCins(0-8h)
End point description:	
Area under the serum insulin lispro concentration-time curve from 0-8 hours	
End point type	Secondary
End point timeframe:	
From t=0 to t=8h after dosing	

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: h.mU/L				
arithmetic mean (standard deviation)	275.31 (± 131.28)	270.76 (± 128.55)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.6099
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.971
upper limit	1.051

Notes:
[6] - Difference

Secondary: Cmax ins

End point title	Cmax ins

End point description:
Maximum observed serum insulin lispro concentration

End point type	Secondary

End point timeframe:
From t=0 to t=8h after dosing

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: mU/L				
arithmetic mean (standard deviation)	125.69 (± 53.013)	110.57 (± 42.921)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.0003
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.061
upper limit	1.198

Notes:
[7] - Differences

Secondary: Tmax ins

End point title	Tmax ins

End point description:
Time to maximum observed serum insulin lispro concentration

End point type	Secondary

End point timeframe:
From t=0 up to t=8h after dosing

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: Hour				
arithmetic mean (standard deviation)	0.818 (± 0.2866)	1.089 (± 0.3935)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.686
upper limit	0.826

Notes:
[8] - Differences

Secondary: T50% early

End point title	T50% early

End point description:
Time to first observed half maximum serum insulin lispro concentration

End point type	Secondary

End point timeframe:
From t=0 up to t=8 hour after dosing

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: hour				
arithmetic mean (standard deviation)	0.318 (± 0.0957)	0.498 (± 0.1443)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.567
upper limit	0.705

Notes:

[9] - Differences

Secondary: T50% late

End point title	T50% late
End point description:	
Time to last observed half maximum serum insulin lispro concentration	
End point type	Secondary
End point timeframe:	
From t=0 up to t=8 hour after dosing	

End point values	BC Lispro	Humalog®		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	38		
Units: hour				
arithmetic mean (standard deviation)	2.367 (± 0.7948)	2.784 (± 0.9348)		

Statistical analyses

Statistical analysis title	BC Lispro vs Humalog®
Comparison groups	BC Lispro v Humalog®
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	LS Mean Ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.785
upper limit	0.911

Notes:

[10] - Differences

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the first IMP (study drug) administration to the safety follow-up visit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	BC Lispro
Reporting group description: -	
Reporting group title	Humalog®
Reporting group description: -	

Serious adverse events	BC Lispro	Humalog®	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (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: 1 %

Non-serious adverse events	BC Lispro	Humalog®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 38 (52.63%)	20 / 38 (52.63%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 38 (7.89%)	2 / 38 (5.26%)	
occurrences (all)	3	2	
Infections and infestations			
nasopharyngitis			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	
occurrences (all)	1	1	
Otitis media			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			

subjects affected / exposed occurrences (all)	0 / 38 (0.00%) 0	1 / 38 (2.63%) 1	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	 18 / 38 (47.37%) 22	 19 / 38 (50.00%) 23	

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