



Clinical trial results:

HEPARINA DE BAJO PESO MOLECULAR (HBPM) para la prevención de complicaciones derivadas de la insuficiencia placentaria en las pacientes de riesgo sin trombofilia: ensayo clínico multicéntrico randomizado

Summary

EudraCT number	2010-023597-39
Trial protocol	ES
Global end of trial date	21 December 2016

Results information

Result version number	v1 (current)
This version publication date	14 October 2021
First version publication date	14 October 2021

Trial information

Trial identification

Sponsor protocol code	HOPPE-Trial
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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, +34 934894779, joaquin.lopez.soriano@vhir.org
Scientific contact	Academic Research Organization, VHIR, aro@vhir.org

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	21 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of treating patients in risk of maternofetal complications

Protection of trial subjects:

Blood analytics were done on 1st, 2nd and 3rd trimester of gestation. In the HBPM group, an additional analytics was done one week after starting treatment. Ecographies were done at 20 and 30-34 weeks of gestation

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 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	Spain: 278
Worldwide total number of subjects	278
EEA total number of subjects	278

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)	278
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	278
Number of subjects completed	278

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The proposal intervention (subcutaneous administration) did not make possible to blind the study

Arms

Are arms mutually exclusive?	Yes
Arm title	LMWH administration

Arm description:

Low Molecular Weight Heparin administration

Arm type	Experimental
Investigational medicinal product name	Heparin
Investigational medicinal product code	
Other name	Sodium Enoxaparin, Clexane
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Daily dose of 40 mg (patients under 80Kg) or 60 mg (patients over 80Kg body weight at inclusion time).
Dose was adjusted over the period, if necessary

Arm title	Control no treatment
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Arm description: -

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	LMWH administration	Control no treatment
Started	144	134
Completed	108	116
Not completed	36	18
Lost to follow-up	31	18
Protocol deviation	5	-

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	278	278	
Age categorical			
Units: Subjects			
Adults (18-64 years)	278	278	
Gender categorical			
Units: Subjects			
Female	278	278	
Male	0	0	

End points

End points reporting groups

Reporting group title	LMWH administration
Reporting group description: Low Molecular Weight Heparin administration	
Reporting group title	Control no treatment
Reporting group description: -	

Primary: Incidence of gestational complications

End point title	Incidence of gestational complications
End point description:	
End point type	Primary
End point timeframe:	
End of gestations	

End point values	LMWH administration	Control no treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	134		
Units: percent				
number (not applicable)	32.0	34.7		

Statistical analyses

Statistical analysis title	Overall complications
Comparison groups	LMWH administration v Control no treatment
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.64
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.85

Secondary: Preeclampsia incidence

End point title	Preeclampsia incidence
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End point description:

End point type	Secondary
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End point timeframe:

All the study

End point values	LMWH administration	Control no treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	134		
Units: percent				
number (not applicable)	7.64	9.70		

Statistical analyses

Statistical analysis title	Preeclampsia
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Comparison groups	LMWH administration v Control no treatment
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Number of subjects included in analysis	278
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Analysis specification	Pre-specified
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Analysis type	non-inferiority
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P-value	= 0.54
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Method	t-test, 2-sided
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Parameter estimate	Odds ratio (OR)
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Point estimate	0.77
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	0.33
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upper limit	1.78
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Secondary: RCIU incidence

End point title	RCIU incidence
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End point description:

End point type	Secondary
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End point timeframe:

All the study

End point values	LMWH administration	Control no treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	134		
Units: percent				
number (not applicable)	12.5	11.2		

Statistical analyses

Statistical analysis title	RCIU incidence
Comparison groups	LMWH administration v Control no treatment
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.736
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	2.35

Secondary: Small foetus

End point title	Small foetus
End point description:	
End point type	Secondary
End point timeframe:	
All the study	

End point values	LMWH administration	Control no treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	134		
Units: percent				
number (not applicable)	10.42	11.19		

Statistical analyses

Statistical analysis title	Small foetus
Comparison groups	LMWH administration v Control no treatment
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.834
Method	t-test, 2-sided
Parameter estimate	Odds ratio (OR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.97

Adverse events

Adverse events information

Timeframe for reporting adverse events:

End of study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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Reporting groups

Reporting group title	Total adverse events
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Reporting group description: -

Serious adverse events	Total adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 278 (2.88%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Intracranial venous thromboembolism			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
HELLP syndrome			
subjects affected / exposed	3 / 278 (1.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Thromboembolism			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
UCI ingress			

subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	2 / 278 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 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	2 / 278 (0.72%)		
Blood and lymphatic system disorders			
Epistaxis			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 278 (0.36%)		
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.

Double blinding was not possible due to nature of intervention. A 19% loss of adherence could make some results. A follow-up of mothers and infants is necessary to evaluate long-term effects of treatment on their health.
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Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/33472201>