Clinical trial results:
An adaptive multicenter, randomized, partially double-blind, placebo-controlled study to assess the safety, PK and PD/efficacy of serelaxin in women with pre-eclampsia

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-001617-14
Trial protocol	DE IT
Global end of trial date	13 August 2014

Results information

Result version number	v1 (current)
This version publication date	04 May 2016
First version publication date	04 May 2016

Trial information

Trial identification

Sponsor protocol code	CRLX030A2205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01566630
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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	13 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 August 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:
•To assess maternal, fetal, and neonatal safety and tolerability of serelaxin at three doses compared to placebo by assessing effects
-on maternal and fetal hemodynamics including systolic blood pressure (SBP) and diastolic blood pressure (DBP), mean arterial pressure (maternal), utero-placental blood flow, and fetal heart rate
-on maternal proteinuria and renal function
-on rate of spontaneous delivery and/or mode of delivery.
-on adverse maternal outcomes
-on fetal cardiotocography and biophysical profile
-on birth weight, gestational age, Appearance, Pulse, Grimace, Activity, Respiration (APGAR) score, umbilical cord gases, and days in neonatal intensive care unit (NICU)
-on adverse fetal/neonatal outcomes
-on safety and tolerability during postpartum follow up (4-6 weeks)
•To investigate PK and development of anti-drug antibodies (maternal/neonatal) after serelaxin and placebo when administered as iv infusion for 72 hours.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial. In case of severe hypertension (SBP ≥ 160mmHg, DBP ≥ 110 mmHg) anti-hypertensives in accordance with standard practice at the study sites could be used to control blood pressure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	3
EEA total number of subjects	1

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)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was terminated with data available for only three patients.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	RLX030

Arm description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. As per planned treatment assigned, patients in this arm received open label serelaxin (RLX030) 15 µg/kg/day i.v. for 72 hours.

Arm type	Experimental
Investigational medicinal product name	Serelaxin
Investigational medicinal product code	RLX030
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

15 µg/kg/day administered intravenously (iv) as infusion for 72 hours to women with pre-eclampsia

Arm title	Placebo

Arm description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. The randomized patient received matching placebo of serelaxin (RLX030) in a blinded manner.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

matching placebo to RLX030 administered intravenously (iv) as infusion for 72 hours to women with pre-eclampsia

Number of subjects in period 1	RLX030	Placebo
Started	2	1
Completed	2	1

Baseline characteristics

Reporting groups	
Reporting group title	RLX030
Reporting group description:	
Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. As per planned treatment assigned, patients in this arm received open label serelaxin (RLX030) 15 µg/kg/day i.v. for 72 hours.	
Reporting group title	Placebo
Reporting group description:	
Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. The randomized patient received matching placebo of serelaxin (RLX030) in a blinded manner.	

Reporting group values	RLX030	Placebo	Total
Number of subjects	2	1	3
Age categorical Units: Subjects			
Adults (18-64 years)	2	1	3
Gender, Male/Female Units: Participants			
Female	2	1	3
Male	0	0	0

End points

End points reporting groups

Reporting group title	RLX030

Reporting group description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. As per planned treatment assigned, patients in this arm received open label serelaxin (RLX030) 15 µg/kg/day i.v. for 72 hours.

Reporting group title	Placebo

Reporting group description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. The randomized patient received matching placebo of serelaxin (RLX030) in a blinded manner.

Subject analysis set title	RLX030 - Maternal
Subject analysis set type	Safety analysis

Subject analysis set description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. Serelaxin (RLX030) 15 µg/kg/day i.v. for 72 hours received by pregnant patients with early onset pre-eclampsia

Subject analysis set title	Placebo - Maternal
Subject analysis set type	Safety analysis

Subject analysis set description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset pre-eclampsia. Matching placebo to serelaxin (RLX030) received for 72 hours by pregnant patients with early onset pre-eclampsia

Subject analysis set title	RLX030- Neonates born to patients
Subject analysis set type	Safety analysis

Subject analysis set description:

Neonates born to patients who received Serelaxin (RLX030) 15 µg/kg/day i.v. for 72 hours received

Subject analysis set title	Placebo- Neonates born to patients
Subject analysis set type	Safety analysis

Subject analysis set description:

Neonates born to patients who received placebo for 72 hours received by pregnant patients with early onset pre-eclampsia

Primary: Number of patients with adverse events, serious adverse and death during part 1 of the study

End point title	Number of patients with adverse events, serious adverse and death during part 1 of the study[1]

End point description:

Safety and tolerability was assessed by adverse events/serious adverse event and death monitoring.

End point type	Primary

End point timeframe:

Prior to delivery until 4-6 weeks post partum (maximum of 8 weeks)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal	RLX030- Neonates born to patients	Placebo- Neonates born to patients
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	1	2	1
Units: Participants				
Serious Adverse events	2	1	2	1
Death	0	0	0	0
Non-serious AEs	2	1	2	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in maternal systolic blood pressure (SBP) and diastolic blood pressure (DBP) in part 1of the study (part 1)

End point title	Change from baseline in maternal systolic blood pressure (SBP) and diastolic blood pressure (DBP) in part 1of the study (part 1)[2]

End point description:

Maternal safety assessment to monitor pre-eclampsia by checking blood pressure during 72 hour treatment period as well as post-dose.

End point type	Primary

End point timeframe:

From baseline to during treatment period of a maximum 72 hours infusion prior to delivery until 4-6 weeks post partum in part 1 (maximum of 8 weeks)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[3]	0[4]		
Units: mmHg				
least squares mean (standard error)	()	()		

Notes:

[3] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[4] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in mean maternal arterial pressure (part 1)

End point title	Change from baseline in mean maternal arterial pressure (part 1)[5]

End point description:

Maternal safety assessment to monitor pre-eclampsia by checking mean arterial pressure during 72 hour treatment period as well as post-dose.

End point type	Primary

End point timeframe:

From baseline to during treatment period of a maximum 72 hours infusion prior to delivery until 4-6 weeks post partum in part 1 (maximum of 8 weeks)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[6]	0[7]		
Units: mmHg				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[7] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline on maternal proteinuria (Part 1)

End point title	Change from baseline on maternal proteinuria (Part 1)[8]

End point description:

Pre-eclampsia was monitored by checking levels of protein in urine and by urinary protein/creatinine ratio (UPCR)

End point type	Primary

End point timeframe:

From baseline to during treatment period of a maximum 72 hours infusion prior to delivery until 4-6 weeks post partum in part 1 (maximum of 8 weeks)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[9]	0[10]		
Units: g/24hr				
arithmetic mean (standard deviation)	()	()		

Notes:

[9] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[10] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Decrease in utero-placental blood flow (Part 1)

End point title	Decrease in utero-placental blood flow (Part 1)[11]

End point description:

Blood flow to the fetus was monitored using via a Doppler.

End point type	Primary

End point timeframe:

During treatment period of a maximum 72 hours infusion prior to delivery and up to delivery in part 1 (maximum of 3 weeks)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[12]	0[13]		
Units: Percentage				
number (not applicable)				

Notes:

[12] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[13] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Change in fetal heart rate (Part 1)

End point title	Change in fetal heart rate (Part 1)[14]

End point description:

Heart rate of fetus was monitored continuously throughout 72 hour treatment period using a cardiotocograph.

End point type	Primary

End point timeframe:

During treatment period of a maximum 72 hours infusion prior to delivery and up to delivery in part 1 (maximum of 3 weeks)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030-Neonates born to patients	Placebo-Neonates born to patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[15]	0[16]		
Units: BPM				
arithmetic mean (standard deviation)	()	()		

Notes:

[15] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[16] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Improvement in renal function assessed by increase in creatinine clearance

End point title	Improvement in renal function assessed by increase in creatinine clearance[17]

End point description:

End point type	Primary

End point timeframe:

From randomization until 4-6 weeks post partum (maximum 8 weeks)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[18]	0[19]		
Units: mL/min/1.73m^2				

Notes:

[18] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[19] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Rate of spontaneous delivery and/or mode of delivery

End point title	Rate of spontaneous delivery and/or mode of delivery[20]

End point description:

End point type	Primary

End point timeframe:

From randomization to delivery (maximum of 3 weeks)

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[21]	0[22]		
Units: Rate				
number (not applicable)				

Notes:

[21] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[22] - No formal analysis was performed as study was terminated after three pts were enrolled and

dosed

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with abnormalities in birth weight, gestational age, Appearance, Pulse, Grimace, Activity, Respiration (APGAR) score, umbilical cord gases, and days in neonatal intensive care unit (NICU)

End point title	Number of patients with abnormalities in birth weight, gestational age, Appearance, Pulse, Grimace, Activity, Respiration (APGAR) score, umbilical cord gases, and days in neonatal intensive care unit (NICU)[23]

End point description:

End point type	Primary

End point timeframe:

up to 4 - 6 weeks post partum (maximum of 8 weeks)

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030-Neonates born to patients	Placebo-Neonates born to patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[24]	0[25]		
Units: Participants				
number (not applicable)				

Notes:

[24] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[25] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with abnormalities in fetal cardiotocography and biophysical profile

End point title	Number of patients with abnormalities in fetal cardiotocography and biophysical profile[26]

End point description:

End point type	Primary

End point timeframe:

Randomization to delivery (maximum of 3 weeks)

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030-Neonates born to patients	Placebo-Neonates born to patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[27]	0[28]		
Units: Participants				
number (not applicable)				

Notes:

[27] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[28] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of RLX030: area under the blood concentration-time curve from time zero to infinity (AUCinf)-Part 1

End point title	Pharmacokinetics of RLX030: area under the blood concentration-time curve from time zero to infinity (AUCinf)-Part 1[29]

End point description:

Blood concentrations of RLX-030 was assayed to determine this PK parameter.

End point type	Primary

End point timeframe:

Baseline, 2, 6, 24,48,72, 76, 80 and 90 hours after initiation of infusion during part 1

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal	RLX030-Neonates born to patients	Placebo-Neonates born to patients
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[30]	0[31]	0[32]	0[33]
Units: ng*hr/mL				

Notes:

[30] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[31] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[32] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[33] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of RLX030: area under the blood concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast)- Part 1

End point title	Pharmacokinetics of RLX030: area under the blood concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast)-Part 1[34]

End point description:

Blood concentrations of RLX-030 was assayed to determine this PK parameter.

End point type	Primary

End point timeframe:

Baseline, 2, 6, 24,48,72, 76, 80 and 90 hours after initiation of infusion during part 1

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal	RLX030- Neonates born to patients	Placebo- Neonates born to patients
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[35]	0[36]	0[37]	0[38]
Units: ng*hr/mL				

Notes:

[35] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[36] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[37] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[38] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of RLX030: blood concentration at 24 hour (C 0-24h) after administration- Part 1

End point title	Pharmacokinetics of RLX030: blood concentration at 24 hour (C 0-24h) after administration- Part 1[39]

End point description:

Blood concentrations of RLX-030 was assayed to determine this PK parameter.

End point type	Primary

End point timeframe:

Baseline, 2, 6, 24,48,72, 76, 80 and 90 hours after initiation of infusion during part 1

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal	RLX030- Neonates born to patients	Placebo- Neonates born to patients
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[40]	0[41]	0[42]	0[43]
Units: ng/mL				

Notes:

[40] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[41] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[42] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[43] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of RLX030: terminal elimination half-life (T1/2)- Part 1

End point title	Pharmacokinetics of RLX030: terminal elimination half-life (T1/2)- Part 1[44]

End point description:

Blood concentrations of RLX-030 was assayed to determine this PK parameter.

End point type	Primary

End point timeframe:

Baseline, 2, 6, 24,48,72, 76, 80 and 90 hours after initiation of infusion during part 1

Notes:

[44] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal	RLX030- Neonates born to patients	Placebo- Neonates born to patients
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[45]	0[46]	0[47]	0[48]
Units: Hours				

Notes:

[45] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[46] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[47] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[48] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetics of RLX030: mean residence time (MRT)

End point title	Pharmacokinetics of RLX030: mean residence time (MRT)[49]

End point description:

Blood concentrations of RLX-030 was assayed to determine this PK parameter.

End point type	Primary

End point timeframe:

Baseline, 2, 6, 24,48,72, 76, 80 and 90 hours after initiation of infusion during part 1

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal	RLX030- Neonates born to patients	Placebo- Neonates born to patients
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[50]	0[51]	0[52]	0[53]
Units: Hours				

Notes:

[50] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[51] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[52] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed
[53] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Primary: Number of Patients With Absence of Anti-serelaxin Antibodies

End point title	Number of Patients With Absence of Anti-serelaxin

End point description:

End point type	Primary

End point timeframe:

From Randomization until 4-6 weeks post partum (maximum of 8 weeks)

Notes:

[54] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was performed as the study was terminated after three patients were enrolled and dosed

End point values	RLX030 - Maternal	Placebo - Maternal	RLX030- Neonates born to patients	Placebo- Neonates born to patients
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[55]	0[56]	0[57]	0[58]
Units: Patients				

Notes:

[55] - No formal analysis was performed as the study was terminated after three patients were enrolled and
[56] - No formal analysis was performed as the study was terminated after three patients were enrolled and
[57] - No formal analysis was performed as the study was terminated after three patients were enrolled and
[58] - No formal analysis was performed as the study was terminated after three patients were enrolled and

Statistical analyses

No statistical analyses for this end point

Secondary: Mean number of days before delivery

End point title	Mean number of days before delivery

End point description:

End point type	Secondary

End point timeframe:

From randomization until delivery (maximum of 3 weeks)

End point values	RLX030 - Maternal	Placebo - Maternal		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[59]	0[60]		
Units: Days				

Notes:

[59] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

[60] - No formal analysis was performed as study was terminated after three pts were enrolled and dosed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	RLX030 - Maternal

Reporting group description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset preeclampsia. Serelaxin (RLX030) 15 µg/kg/day i.v. for 72 hours received by pregnant patients with early onset pre-eclampsia

Reporting group title	RLX030 - Neonates Born to Patients

Reporting group description:

Neonates born to patients who received Serelaxin (RLX030) 15 µg/kg/day i.v. for 72 hours received

Reporting group title	Placebo - Maternal

Reporting group description:

Because premature termination of the study, only Cohort 1 part 1 had patients with early onset preeclampsia. Matching placebo to serelaxin (RLX030) received for 72 hours by pregnant patients with early onset pre-eclampsia

Reporting group title	Placebo - Neonates Born to Patients

Reporting group description:

Neonates born to patients who received placebo for 72 hours received by pregnant patients with early onset pre-eclampsia

Serious adverse events	RLX030 - Maternal	RLX030 - Neonates Born to Patients	Placebo - Maternal
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	1 / 1 (100.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Caesarean section			

subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pre-eclampsia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature baby			
subjects affected / exposed	0 / 2 (0.00%)	2 / 2 (100.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature delivery			
subjects affected / exposed	2 / 2 (100.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo - Neonates Born to Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Caesarean section			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pre-eclampsia			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Premature baby			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Premature delivery			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	RLX030 - Maternal	RLX030 - Neonates Born to Patients	Placebo - Maternal
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	1 / 1 (100.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Surgical and medical procedures			
Mechanical ventilation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	1	0	1
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Apnoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Epistaxis			

subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Transient tachypnoea of the newborn			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo - Neonates Born to Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Mechanical ventilation			

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0		
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Hepatobiliary disorders Jaundice subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Acute respiratory distress syndrome subjects affected / exposed occurrences (all) Apnoea subjects affected / exposed occurrences (all) Dyspnoea	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Transient tachypnoea of the newborn			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

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.

Novartis terminated this study due to internal, strategic decisions

Notes: