



Clinical trial results:

A Two Part, Phase 2 Open-label, Multi-Centre, Dose Escalation Hemodynamic Study to Evaluate Dose-Response and Safety of Inhaled LIQ861 (Treprostinil) in Pulmonary Arterial Hypertension (WHO Group 1) Subjects

Summary

EudraCT number	2018-003414-40
Trial protocol	DE FR
Global end of trial date	12 May 2021

Results information

Result version number	v1 (current)
This version publication date	25 August 2022
First version publication date	25 August 2022
Summary attachment (see zip file)	LTI-201 Summary (LTI-201_CSRSv1-0_20220502.pdf)

Trial information

Trial identification

Sponsor protocol code	LTI-201
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Liquidia Technologies, Inc
Sponsor organisation address	419 Davis Dr., Suite 100, Morrisville, NC, United States, 27560
Public contact	Liquidia Technologies Headquarters, Liquidia Technologies, Inc., +1 919 328-4400, ClinicalTrials@liquidia.com
Scientific contact	Liquidia Technologies Headquarters, Liquidia Technologies, Inc., +1 919 328-4400, ClinicalTrials@liquidia.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	26 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2021
Global end of trial reached?	Yes
Global end of trial date	12 May 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to characterize hemodynamic dose-response relationships for LIQ861.

Protection of trial subjects:

Subject signed Informed Consent; Protocol was approved by Ethic Committees and Regulatory Authorities and we adhered to all ICH guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 January 2019
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: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	11
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients in the LTI-201 study were from PAH centers in France (enrolled 0) and Germany (enrolled 15) from October 30, 2019 (first patient screened) thru December 7, 2020 (last patient screened).

Pre-assignment

Screening details:

The following screening assessments were performed to assess eligibility criteria:

Record medical history, demographics, comeds, vital signs, functional class assessment, height and weight.

Blood was drawn for laboratory assessment and pulmonary function testing performed.

6 Minute Walk test was collected for study eligibility.

Period 1

Period 1 title	Part A
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 - Day 1

Arm description:

Cohort 1 - Day 1 received 5 mg of LIQ861

Arm type	Experimental
Investigational medicinal product name	treprostinil
Investigational medicinal product code	LIQ861 5 mg
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

Dosage: LIQ861 5 mg capsule contains 26.5 mcg treprostinil

Mode of administration: dry powder inhalation by using the RS00 Model 8 dry-powder inhaler

Arm title	Cohort 2 - Day 1
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Arm description:

LIQ861 10 mg Day 1

Arm type	Experimental
Investigational medicinal product name	treprostinil
Investigational medicinal product code	LIQ861 10 mg
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

Dosage: LIQ861 10 mg capsule contains 53 mcg treprostinil

Mode of administration: dry powder inhalation by using the RS00 Model 8 dry-powder inhaler

Number of subjects in period 1	Cohort 1 - Day 1	Cohort 2 - Day 1
Started	8	7
Completed	8	7

Period 2

Period 2 title	Part B
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Cohort 2 - Day 1

Arm description:

LIQ861 10 mg Day 1

Arm type	Experimental
Investigational medicinal product name	treprostinil
Investigational medicinal product code	LIQ861 10 mg
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

Dosage: LIQ861 10 mg capsule contains 53 mcg treprostinil

Mode of administration: dry powder inhalation by using the RS00 Model 8 dry-powder inhaler

Arm title	Cohort 2 - Week 16
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Arm description:

LIQ861 10 mg - Week 16

Arm type	Experimental
Investigational medicinal product name	treprostinil
Investigational medicinal product code	LIQ861
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Inhalation use

Dosage and administration details:

Dosage: Subjects titrated to symptom relief (dosed between 5 mg and 30 mg LIQ861)

Mode of administration: dry powder inhalation by using the RS00 Model 8 dry-powder inhaler

Number of subjects in period 2	Cohort 2 - Day 1	Cohort 2 - Week 16
Started	7	7
Completed	7	0
Not completed	0	7
Early Termination of Study	-	7

Baseline characteristics

End points

End points reporting groups

Reporting group title	Cohort 1 - Day 1
Reporting group description: Cohort 1 - Day 1 received 5 mg of LIQ861	
Reporting group title	Cohort 2 - Day 1
Reporting group description: LIQ861 10 mg Day 1	
Reporting group title	Cohort 2 - Day 1
Reporting group description: LIQ861 10 mg Day 1	
Reporting group title	Cohort 2 - Week 16
Reporting group description: LIQ861 10 mg - Week 16	
Subject analysis set title	Cohort 1
Subject analysis set type	Full analysis
Subject analysis set description: Group of patient's dosed with 5 mg of LIQ861	
Subject analysis set title	Cohort 2
Subject analysis set type	Per protocol
Subject analysis set description: Subjects received 10 mg of LIQ861. Only Day 1 data is available as study was terminated early.	

Primary: Pulmonary Vascular Resistance - Day 1

End point title	Pulmonary Vascular Resistance - Day 1 ^[1]
End point description: The change in PVR measured from Baseline (pre-dose) to maximal response (eMAX) at Day 1 will be considered the primary efficacy endpoint.	
End point type	Primary
End point timeframe: Day 1	

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 statistical testing was done. All variables were analyzed descriptively, ie, continuous variables by summary statistics and categorical variables by frequency tables using number and percentage of subjects.

End point values	Cohort 1	Cohort 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: dynes/sec/cm-5				
arithmetic mean (standard error)	-143.3 (± 24.1)	-139.1 (± 39.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Incidence and Severity of AEs

End point title	Incidence and Severity of AEs ^[2]
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End point description:

The primary safety endpoint in Parts A and B and the open-label extension period will be the incidence and severity of AEs and Serious Adverse Events (SAEs) grouped by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class, dose level, time on drug, and relationship to dose.

End point type	Primary
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End point timeframe:

Safety endpoints changes from Day 1 to end of treatment.

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 statistical testing was done. All variables were analyzed descriptively, ie, continuous variables by summary statistics and categorical variables by frequency tables using number and percentage of subjects.

End point values	Cohort 1	Cohort 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: Incidence	27	15		

Statistical analyses

No statistical analyses for this end point

Primary: Pulmonary Vascular Resistance - Week 16

End point title	Pulmonary Vascular Resistance - Week 16 ^[3]
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End point description:

The change in PVR measured from Baseline (pre-dose) to maximal response (eMAX) at Week 16 will be considered the primary efficacy endpoint.

End point type	Primary
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End point timeframe:

Week 16

Notes:

[3] - 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 statistical testing was done. All variables were analyzed descriptively, ie, continuous variables by summary statistics and categorical variables by frequency tables using number and percentage of subjects.

End point values	Cohort 1			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: dynes/sec/cm-5				
arithmetic mean (standard error)	-137 (± 54.9)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Pulmonary Arterial Pressure - Day 1

End point title	Mean Pulmonary Arterial Pressure - Day 1
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End point description:

End point type	Other pre-specified
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End point timeframe:

Day 1

End point values	Cohort 1	Cohort 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: mmHg				
arithmetic mean (standard error)	-7.3 ($\pm$ 2.4)	-8.4 ($\pm$ 2.8)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PK Parameters: Cmax

End point title	PK Parameters: Cmax
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End point description:

End point type	Other pre-specified
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End point timeframe:

Day 1

End point values	Cohort 1	Cohort 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: ng/ml				
geometric mean (full range (min-max))	0.213 (.128 to 0.347)	0.496 (0.305 to 0.909)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PK Parameters: AUC (tau)

End point title	PK Parameters: AUC (tau)
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End point description:

End point type	Other pre-specified
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End point timeframe:

Day 1

End point values	Cohort 1	Cohort 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: H*ng/ml				
geometric mean (full range (min-max))	0.198 (0.127 to 0.390)	0.469 (0.261 to 0.841)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean Pulmonary Arterial Pressure - Week 16

End point title	Mean Pulmonary Arterial Pressure - Week 16
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End point description:

End point type	Other pre-specified
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End point timeframe:

Week 16

End point values	Cohort 1			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: mmHg				
arithmetic mean (standard error)	-9.0 ($\pm$ 4.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to 30 days after end of treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	Cohort 1
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Reporting group description: -

Reporting group title	Cohort 2
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Reporting group description: -

Serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	6 / 7 (85.71%)	
Investigations			
Brain natriuretic peptide increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	1 / 7 (14.29%) 1	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	2 / 8 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 8 (50.00%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	1 / 8 (12.50%)	3 / 7 (42.86%)	
occurrences (all)	1	3	

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.

The study was prematurely terminated due to the impact of COVID on recruitment. Due to the early termination, only the first two cohorts were enrolled and the LIQ861 dose of subjects in Part B was down titrated at the investigator's discretion.
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