Clinical trial results:
A Multicenter, Open-Label Study to Evaluate the Pharmacokinetics, Tolerability, and Safety of a Single Dose of Staccato Alprazolam in Adolescent Study Participants With Epilepsy

Summary

EudraCT number	2022-002523-36
Trial protocol	Outside EU/EEA
Global end of trial date	05 April 2022

Results information

Result version number	v1 (current)
This version publication date	28 September 2022
First version publication date	28 September 2022

Trial information

Trial identification

Sponsor protocol code	UP0100

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04857307
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-003043-PIP01-21
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	05 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 April 2022
Global end of trial reached?	Yes
Global end of trial date	05 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the pharmacokinetic (PK) of alprazolam in adolescent study participants with epilepsy following single inhaled dose of Staccato alprazolam

• To evaluate the safety and tolerability of Staccato alprazolam in adolescent study participants with epilepsy

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	28 April 2021
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	United States: 14
Worldwide total number of subjects	14
EEA total number of subjects	0

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)	14
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll study participants in April 2021 and concluded in April 2022.

Pre-assignment

Screening details:

Participant Flow refers to the Safety Set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Staccato Alprazolam

Arm description:

Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9.

Arm type	Experimental
Investigational medicinal product name	Staccato Alprazolam
Investigational medicinal product code	UCB7538
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received staccato alprazolam on Day 1.

Number of subjects in period 1	Staccato Alprazolam
Started	14
Completed	14

Baseline characteristics

Reporting groups	
Reporting group title	Staccato Alprazolam
Reporting group description:	
Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9.	

Reporting group values	Staccato Alprazolam	Total	
Number of subjects	14	14	
Age Categorical Units: participants			
<=18 years	14	14	
Between 18 and 65 years	0	0	
>=65 years	0	0	
Age Continuous Units: years			
arithmetic mean	15.1		
standard deviation	± 1.9	-	
Sex: Female, Male Units: participants			
Female	12	12	
Male	2	2	

End points

End points reporting groups

Reporting group title	Staccato Alprazolam

Reporting group description:

Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9.

Primary: Maximum plasma concentration (Cmax) following single inhaled dose of Staccato alprazolam

End point title	Maximum plasma concentration (Cmax) following single inhaled dose of Staccato alprazolam[1]

End point description:

Cmax was defined as the maximum observed plasma concentration. Pharmacokinetic Set (PKS) included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement.

End point type	Primary

End point timeframe:

Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour, 2 hours, 6 hours, 24 hours, and 36 hours postdose

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 hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Staccato Alprazolam			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: nanogram/milliliter				
geometric mean (geometric coefficient of variation)	35.50 (± 57.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from zero to the last quantifiable concentration (AUC(0-t)) following single inhaled dose of Staccato alprazolam

End point title	Area under the plasma concentration-time curve from zero to the last quantifiable concentration (AUC(0-t)) following single inhaled dose of Staccato alprazolam[2]

End point description:

AUC(0-t) was defined as area under the plasma concentration-time curve from zero to the last quantifiable concentration. Pharmacokinetic Set included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement.

End point type	Primary

End point timeframe:

Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour,

2 hours, 6 hours, 24 hours, and 36 hours postdose

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 hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Staccato Alprazolam			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: hour*nanogram/milliliter				
geometric mean (geometric coefficient of variation)	278.2 (± 36.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from time 0 to infinity (AUC) following single inhaled dose of Staccato alprazolam

End point title	Area under the plasma concentration-time curve from time 0 to infinity (AUC) following single inhaled dose of Staccato alprazolam[3]

End point description:

AUC was defined as area under the plasma concentration-time curve from time 0 to infinity. Pharmacokinetic Set included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour, 2 hours, 6 hours, 24 hours, and 36 hours postdose

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 hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Staccato Alprazolam			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: hour*nanogram/milliliter				
geometric mean (geometric coefficient of variation)	280.0 (± 35.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent total body clearance (CL/F) following single inhaled dose of

Staccato alprazolam

End point title	Apparent total body clearance (CL/F) following single inhaled dose of Staccato alprazolam[4]

End point description:

CL/F was defined as apparent total body clearance. Pharmacokinetic Set included all study participants who received at least 1 dose of IMP and had at least 1 observable PK measurement. Here, Number of Participants Analyzed signifies those participants who were evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Plasma samples were taken on Day 1, predose and then at 2 minutes, 10 minutes, 30 minutes, 1 hour, 2 hours, 6 hours, 24 hours, and 36 hours postdose

Notes:

[4] - 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 hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Staccato Alprazolam			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Liter/hour				
geometric mean (geometric coefficient of variation)	7.144 (± 35.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with treatment-emergent adverse events (TEAEs)

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs)[5]

End point description:

A TEAE was defined as any AE with a start date/time on or after the dose of treatment or any unresolved event already present before administration of treatment that worsened in intensity following exposure to the treatment. Safety Set consisted of all study participants who received at least 1 dose of IMP.

End point type	Primary

End point timeframe:

From Baseline (Day 1) till end of Safety Follow-up (up to Day 9)

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 statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Staccato Alprazolam			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: percentage of participants				
number (not applicable)	21.4			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with serious treatment-emergent adverse events (serious TEAEs)

End point title	Percentage of participants with serious treatment-emergent adverse events (serious TEAEs)[6]

End point description:

A TEAE was defined as any AE with a start date/time on or after the dose of treatment or any unresolved event already present before administration of treatment that worsened in intensity following exposure to the treatment. A serious adverse event (SAE) was defined as any untoward medical occurrence that, at any dose: a. Resulted in death, b. Is life-threatening, c. Required inpatient hospitalization or prolongation of existing hospitalization, d. Resulted in persistent disability/incapacity, e. Is a congenital anomaly/birth defect, f. Important medical events. Safety Set consisted of all study participants who received at least 1 dose of IMP.

End point type	Primary

End point timeframe:

From Baseline (Day 1) till end of Safety Follow-up (up to Day 9)

Notes:

[6] - 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 hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Staccato Alprazolam			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline (Day 1) till end of Safety Follow-up (up to Day 9)

Adverse event reporting additional description:

A TEAE was defined as any AE with a start date/time on or after the dose of treatment or any unresolved event already present before administration of treatment that worsened in intensity following exposure to the treatment. Safety Set was analyzed for TEAEs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Staccato Alprazolam

Reporting group description:

Participants received staccato alprazolam inhalation powder on Day 1. Participants were followed up to Day 9.

Serious adverse events	Staccato Alprazolam		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Staccato Alprazolam		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 14 (21.43%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Somnolence			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	4		
Dizziness			

subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Hiccups subjects affected / exposed occurrences (all)	 2 / 14 (14.29%) 2 2 / 14 (14.29%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2022	Protocol Amendment 3, dated 12 Jan 2022, was a substantial amendment that was implemented after 6 participants had been enrolled in the study. The main purpose of this amendment was to decrease the burden on study participants, their families, and clinical sites by allowing study participants to leave the clinic after the 6-hour postdose safety assessments and PK blood sampling and return to the clinic for the 24- and 36-hour postdose assessments, at the discretion of the Investigator. This change in the study conduct was supported by results from the first set of study participants (N=6, including at least 2 adolescent participants with body weight <50kg) enrolled in UP0100. Careful review of these results by the study safety monitoring committee (SMC) did not reveal any safety concerns that would preclude discharge of UP0100 study participants after the 6-hour postdose assessments. Edits were made to clarify removal of the 12-hour time point for assessment of vital signs, peripheral oxygen saturation (SpO2), and sedation/sleepiness (by visual analog scale [VAS]) from the Schedule of Assessments and other applicable sections of the protocol.

Notes:

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 PK endpoint measures of geometric mean are presented with percentage geometric coefficients of variation.

Notes: