Clinical trial results:
A MULTICENTER, OPEN-LABEL STUDY TO INVESTIGATE THE SAFETY AND TOLERABILITY OF INTRAVENOUS LACOSAMIDE IN CHILDREN (1 MONTH TO <17 YEARS OF AGE) WITH EPILEPSY

Summary

EudraCT number	2014-003294-42
Trial protocol	HU IT DE PL
Global end of trial date	28 June 2019

Results information

Result version number	v2 (current)
This version publication date	09 August 2020
First version publication date	12 January 2020
Version creation reason	• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review.

Trial information

Trial identification

Sponsor protocol code	EP0060

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02710890
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB BIOSCIENCES Inc
Sponsor organisation address	8010 Arco Corporate Drive, Raleigh, United States, NC 27617
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)	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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2019
Global end of trial reached?	Yes
Global end of trial date	28 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of intravenous (iv) lacosamide (LCM) infusion(s) in pediatric participants >=1 month to <17 years with epilepsy

Protection of trial subjects:

During the conduct of 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	30 May 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Ukraine: 42
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	103
EEA total number of subjects	35

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)	12

Children (2-11 years)	56
Adolescents (12-17 years)	35
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 participants in May 2017 and concluded in June 2019.

Pre-assignment

Screening details:

Participant Flow refers to the Safety Set iv (SS-iv).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Lacosamide Age Cohort ≥ 1 month - < 8 years

Arm description:

This arm consisted of participants who formed Cohort 2, were greater than or equal to (≥) 1 month to less than (<) 8 years of age and received at least 1 dose of intravenous (iv) lacosamide (LCM). For the first 20 participants in Cohort 2, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 2, a Data Monitoring Committee (DMC) reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated.

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	LCM
Other name	Vimpat
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LCM solution for infusion in glass iv vials (10 mg/mL in a 20 mL vial; each vial contained LCM 200 mg). The first iv LCM dose was given on Day 1. If more than 1 infusion was given, iv LCM was administered bid at approximately 12-hour intervals, once in the morning and once in the evening, for up to 10 doses (or up to 5 days) for clinical need administration or up to 2 consecutive doses (over approximately 24 hours) for elective administration.

Arm title	Lacosamide Age Cohort ≥ 8 - < 17 years

Arm description:

This arm consisted of participants who formed Cohort 1, were ≥ 8 to < 17 years of age and received at least 1 dose of iv LCM. For the first 20 participants in Cohort 1, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 1, a DMC reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated, and progression to initiate enrollment in the next Cohort (Cohort 2).

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	LCM
Other name	Vimpat
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LCM solution for infusion in glass iv vials (10 mg/mL in a 20 mL vial; each vial contained LCM 200 mg). The first iv LCM dose was given on Day 1. If more than 1 infusion was given, iv LCM was administered

bid at approximately 12-hour intervals, once in the morning and once in the evening, for up to 10 doses (or up to 5 days) for clinical need administration or up to 2 consecutive doses (over approximately 24 hours) for elective administration.

Number of subjects in period 1	Lacosamide Age Cohort ≥ 1 month - < 8 years	Lacosamide Age Cohort ≥ 8 - < 17 years
Started	48	55
Completed	48	55

Baseline characteristics

Reporting groups

Reporting group title	Lacosamide Age Cohort ≥ 1 month - < 8 years

Reporting group description:

This arm consisted of participants who formed Cohort 2, were greater than or equal to (≥) 1 month to less than (<) 8 years of age and received at least 1 dose of intravenous (iv) lacosamide (LCM). For the first 20 participants in Cohort 2, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 2, a Data Monitoring Committee (DMC) reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated.

Reporting group title	Lacosamide Age Cohort ≥ 8 - < 17 years

Reporting group description:

This arm consisted of participants who formed Cohort 1, were ≥ 8 to < 17 years of age and received at least 1 dose of iv LCM. For the first 20 participants in Cohort 1, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 1, a DMC reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated, and progression to initiate enrollment in the next Cohort (Cohort 2).

Reporting group values	Lacosamide Age Cohort ≥ 1 month - < 8 years	Lacosamide Age Cohort ≥ 8 - < 17 years	Total
Number of subjects	48	55	103
Age categorical Units: Subjects			
<=18 years	48	55	103
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Age continuous Units: years			
arithmetic mean	3.840	12.662	
standard deviation	± 2.329	± 2.409	-
Gender categorical Units: Subjects			
Male	22	24	46
Female	26	31	57

End points

End points reporting groups

Reporting group title	Lacosamide Age Cohort ≥ 1 month - < 8 years

Reporting group description:

This arm consisted of participants who formed Cohort 2, were greater than or equal to (≥) 1 month to less than (<) 8 years of age and received at least 1 dose of intravenous (iv) lacosamide (LCM). For the first 20 participants in Cohort 2, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 2, a Data Monitoring Committee (DMC) reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated.

Reporting group title	Lacosamide Age Cohort ≥ 8 - < 17 years

Reporting group description:

This arm consisted of participants who formed Cohort 1, were ≥ 8 to < 17 years of age and received at least 1 dose of iv LCM. For the first 20 participants in Cohort 1, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 1, a DMC reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated, and progression to initiate enrollment in the next Cohort (Cohort 2).

Subject analysis set title	Lacosamide Age Cohort ≥ 1 month - < 8 years (SS-iv)
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of participants who formed Cohort 2, were ≥ 1 month to < 8 years of age and received at least 1 dose of iv LCM. For the first 20 participants in Cohort 2, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 2, a DMC reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated. Participants formed the Safety Set iv (SS-iv).

Subject analysis set title	Lacosamide Age Cohort ≥ 8 - < 17 years (SS-iv)
Subject analysis set type	Safety analysis

Subject analysis set description:

This arm consisted of participants who formed Cohort 1, were ≥ 8 to < 17 years of age and received at least 1 dose of iv LCM. For the first 20 participants in Cohort 1, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 1, a DMC reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated, and progression to initiate enrollment in the next Cohort (Cohort 2). Participants formed the Safety Set iv (SS-iv).

Primary: Percentage of participants with at least one adverse event reported spontaneously by the participant/or caregiver (including parent/legal guardian) or observed by the investigator during the study

End point title	Percentage of participants with at least one adverse event reported spontaneously by the participant/or caregiver (including parent/legal guardian) or observed by the investigator during the study[1]

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

26 adverse events are reported splitting into at least 19 occurrences of individual pre-treatment emergent adverse events and 7 treatment emergent adverse events (TEAEs).

End point type	Primary

End point timeframe:

From Screening Period (Day -7 to Day -1) up to the End-of-Study Period (up to Day 37)

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 as descriptive statistics only.

End point values	Lacosamide Age Cohort ≥ 1 month - < 8 years (SS-iv)	Lacosamide Age Cohort ≥ 8 - < 17 years (SS-iv)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	55		
Units: percentage of participants				
number (not applicable)	12.5	14.5		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants that withdrew due to adverse events during the study

End point title	Percentage of participants that withdrew due to adverse events during the study[2]

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment and led to the withdrawal of the participants from the study. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

End point type	Primary

End point timeframe:

From Screening Period (Day -7 to Day -1) up to the End-of-Study Period (up to Day 37)

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 as descriptive statistics only.

End point values	Lacosamide Age Cohort ≥ 1 month - < 8 years (SS-iv)	Lacosamide Age Cohort ≥ 8 - < 17 years (SS-iv)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	55		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment Emergent Adverse Events were reported from Visit 2/Day 1 until End of Study Period (29 to 37 days after Visit 2/Day 1).

Adverse event reporting additional description:

1 participant could experience multiple adverse events.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Lacosamide Age Cohort ≥ 1 month - < 8 years (SS-iv)

Reporting group description:

This arm consisted of participants who formed Cohort 2, were ≥ 1 month to < 8 years of age and received at least 1 dose of iv LCM. For the first 20 participants in Cohort 2, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 2, a DMC reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated. Participants formed the Safety Set iv (SS-iv).

Reporting group title	Lacosamide Age Cohort ≥ 8 - < 17 years (SS-iv)

Reporting group description:

This arm consisted of participants who formed Cohort 1, were ≥ 8 to < 17 years of age and received at least 1 dose of iv LCM. For the first 20 participants in Cohort 1, iv LCM has been infused over a duration of 30 minutes but no longer than 60 minutes whenever possible. After completion of the first 20 participants in Cohort 1, a DMC reviewed the safety and tolerability data for this Cohort and made the following recommendations: the progression of the current Cohort, including iv infusion durations to be evaluated, and progression to initiate enrollment in the next Cohort (Cohort 2). Participants formed the Safety Set iv (SS-iv).

Serious adverse events	Lacosamide Age Cohort ≥ 1 month - < 8 years (SS-iv)	Lacosamide Age Cohort ≥ 8 - < 17 years (SS-iv)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (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: 0 %

Non-serious adverse events	Lacosamide Age Cohort ≥ 1 month - < 8 years (SS-iv)	Lacosamide Age Cohort ≥ 8 - < 17 years (SS-iv)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 48 (6.25%)	2 / 55 (3.64%)	

Investigations			
Blood triglycerides increased			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	
occurrences (all)	0	2	
Blood cholesterol increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Functional gastrointestinal disorder			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2015	Protocol Amendment 1, dated 21 Jul 2015, provided the following key changes. The primary purpose of this substantial amendment was to provide further clarification regarding the design of the study, the definition of the clinical situation in which a study participant was qualified for enrollment in this study, and the pharmacokinetic(s) (PK) assessments in accordance with the United States (US) Food and Drug Administration (FDA) request. It was clarified that this study enrolls approximately 75 study participants ≥4 to <17 years of age and that another Phase 2/3 study was planned to investigate the use of intravenous (iv) lacosamide (LCM) in study participants with epilepsy ≥1 month to <4 years of age. EP0060 initially enrolled older pediatric study participants (Cohort 1), which includes at least 20 study participants ≥12 to <17 years of age. After the first 10 study participants in each cohort completed their iv LCM treatment over infusion durations of 30 to 60 minutes, the enrollment was temporarily put on hold for the Independent Data Monitoring Committee (IDMC) to review the available safety and tolerability data. Additional changes were implemented for consistency with other protocols in the LCM pediatric program. Furthermore, administrative changes including the update of the study team and update of the Sponsor Declaration were made. At the time of approval of this amendment, no study participants were enrolled in EP0060.
30 November 2016	Protocol Amendment 2, dated 30 Nov 2016, provided the following key changes. The primary purpose of this substantial amendment was to maximize the patient pool used in the evaluation of the safety of iv LCM in pediatric study participants. Thus, enrollment was opened to include open-label lacosamide (OLL) and prescribed lacosamide (RxL) study participants who are on a stable dose of oral LCM and elect to receive iv LCM as well as initiating intravenous lacosamide (IIL) study participants who are not currently taking LCM and initiate adjunctive LCM treatment using iv LCM. This amendment also included the option for RxL and IIL study participants to continue oral LCM treatment in SP848, if clinically appropriate, after completion of iv LCM in EP0060. Given this option for RxL and IIL study participants, 2 visits were added to the study design. If required, a Transition Visit was added for RxL and IIL study participants transitioning to SP848 and requiring up to 7 days for scheduling of additional assessments to be performed during EP0060. If not transitioning to SP848, an additional Safety Follow-Up (SFU) Telephone Contact Visit was added approximately 30 days after last infusion to collect final safety data. In order to provide treatment continuity, a short-term oral LCM solution may have been dispensed to RxL and IIL study participants eligible for SP848 enrollment in the event that additional time was needed to schedule the Transition Visit. Enrollment from EP0012 was removed as well as enrollment from future pediatric studies.

30 November 2016	- Continuation 1 - The study design was changed to merge the previous Cohort 1 (≥12 to <17 years of age) and Cohort 2 (≥8 to <12 years of age) into 1 cohort spanning the age range of ≥8 to <17 years of age while maintaining the combined planned enrollment for this age group. The decision to combine these 2 age groups was supported by the following 3 considerations: PK modeling, growth chart information, postmarketing safety assessment of iv LCM use, and a recent publication (Arkilo, et al 2016). • In the oral and iv LCM PK pediatric modeling CL0266, simulations of iv LCM infused over durations of 15 to 60 minutes suggested that exposure was similar to oral administration. These results were consistent with the LCM PK profile and bioequivalence of iv and oral LCM established in adults. Thus, using the weight-based dosing adaptations for LCM adjunctive therapy, it was predicted that the LCM concentration at steady-state in pediatric study participants with partial-onset seizures would be similar to that in adults for both oral and iv LCM. Based on the PK modeling, the use of iv LCM was expected to be safe in the pediatric patient population down to 4 years of age. • Based on the Centers for Disease Control and Prevention (CDC) growth charts for weight-for-age percentiles (2 years to 20 years of age), the ages at which a child reaches the 50th percentile at a weight of 50kg are 13.82 years for boys and 14.21 years for girls (http://www.cdc.gov/growthcharts, 2000). Therefore, average pediatric patients weighing 50kg are approximately 2 to 3 years younger than the currently approved lower limit for age for VIMPAT (16 years [EU] or 17 years [US]). Based on PK modeling, LCM exposure in pediatric study participants weighing 50kg or more was predicted to be the same as exposure observed in adults.
30 November 2016	- Continuation 2 - • Postmarketing data were evaluated for the period from 01 Aug 2008 to 30 Nov 2015, and 49 cases were identified for iv LCM formulation use in the pediatric population (in patients 4 to <16 years of age). Based on review of these cases, no new safety concerns were identified. • Arkilo and colleagues examined use of iv LCM in 47 infants and children from 4 months to <12 years of age, and this study included use in nonapproved indications (ie, status epilepticus) (Arkilo, et al 2016). Evaluation of adverse effects was not possible for the 11 study participants in status epilepticus. Five of remaining 36 study participants experienced sedation, and no new safety concerns were noted in this evaluation. Taken together, along with current knowledge of the safety of oral LCM in children down to 4 years of age, enrollment of children ≥8 to <17 years of age within the same cohort were expected not to present a significant safety risk and to allow earlier benefit of access to the iv LCM option of treatment for those study participants who were ≥8 to <12 years of age. Initiation of the assessment of safety in patients ≥4 to <8 year olds remained dependent on review of safety data from Cohort 1 by the IDMC. To accommodate these changes, revisions were made to the inclusion/exclusion criteria, schedule of assessments, LCM dosing, and statistical analyses. Additional changes were implemented for consistency with other protocols in the LCM pediatric program and updated language in protocol template regarding monitoring for potential drug-induced liver injury (PDILI) events. Furthermore, administrative changes including the update of the study team were made. At the time of approval of this amendment, no study participants were enrolled in EP0060.

30 April 2018	Protocol Amendment 3, dated 30 Apr 2018, provided the following key changes. The primary purpose of this substantial amendment was to lower the age of study participants from ≥4 years to ≥1 month in an effort to maximize the study participant pool in the evaluation of iv LCM, to include age stratification within Cohort 2 to be most informative with regard to safety and PK, and to increase study enrollment from 75 to 100 study participants to reflect the inclusion of study participants down to 1 month of age. Since the initial conception of the study, substantial new safety and efficacy information on the lowest age group (≥1 month to <4 years of age) was published. The available safety information consisted of postmarketing data (n=27 patient cases), data from internal studies (n=15 patient cases), as well as from 2 published reports (n=15 and n=22 patient cases) (Arkilo et al, 2016; Welsh et al, 2017, respectively). These reports covered the age range from ≥1 month to <4 years of age and also covered the clinical spectrum from an open-label extension study with oral treatment to critical care patients receiving iv treatment. This data pointed to no specific risks in the age group after administration of VIMPAT and UCB, therefore, believed it was justified to open Cohort 2 to the lowest age group in agreement with the IDMC outcome on safety of Cohort 1. To accommodate these changes, revisions were made to the inclusion/exclusion criteria, schedule of assessments, LCM dosing, and statistical analyses. Additional changes included the following: • Study contact information was updated as applicable. • Additional region to maximize enrollment was included. • Number of study participants included in the IDMC process in Cohort 2 was modified. • The timing of the End-of-Study/Final Visit was clarified. • Wording regarding the taper of LCM for IIL study participants who discontinue use was removed. • US and EU regulatory authority approvals of LCM were updated.
30 April 2018	- Continuation 1 - • Pharmacokinetic variables were further defined as "Other". • Bicarbonate testing was optional for study participants weighing less than 8kg. • New inclusion criterion was added for all study participants. • New exclusion criterion was added for RxL and IIL study participants. • Oral LCM was to be administered approximately 12 hours after the final iv LCM infusion was clarified. • Potential drug-induced liver injury language was updated to most current UCB template. • List of hematology PDILI laboratory measurements was updated. • List of chemistry PDILI laboratory measurements was updated. • Clarification was added regarding the reading of 12-lead electrocardiogram (ECG). • Definitions of analysis sets were modified. • Data presentations for planned PK and safety analyses were revised. • Minor typographical errors and clarifications were made and are not listed in the summary of changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported