



## Clinical trial results:

### A Feasibility Randomised Controlled Trial: Effects of Oral Sodium Bicarbonate Supplementation in Patients on Haemodialysis

#### Summary

EudraCT number	2015-001439-20
Trial protocol	GB
Global end of trial date	03 May 2016

#### Results information

Result version number	v1 (current)
This version publication date	03 January 2020
First version publication date	03 January 2020

#### Trial information

##### Trial identification

Sponsor protocol code	15HH2613
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02692378
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Imperial College Healthcare NHS Trust
Sponsor organisation address	Du Cane Road, London, United Kingdom, W12 0HS
Public contact	Dr Damien Ashby , Imperial College Healthcare NHS Trust , +44 02033135171, damien.ashby@nhs.net
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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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	03 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2016
Global end of trial reached?	Yes
Global end of trial date	03 May 2016
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

Principal research question:

What are the effects of oral sodium bicarbonate supplementation in haemodialysis patients?

Principal objective:

Investigate the effect of oral sodium bicarbonate supplementation on blood potassium levels throughout the dialysis cycle (pre and post dialysis potassium and intradialysis potassium gradient).

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Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	United Kingdom: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

Notes:

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**Subjects enrolled per age group**

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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)	28
From 65 to 84 years	15

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited from three satellite haemodialysis units at Imperial NHS Trust between June 2015 and May 2016.

### Pre-assignment

Screening details:

518 patients were screened and 130 were eligible for enrolment, finally enrolled 43 patients.

### Period 1

Period 1 title	Run-in phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Control

Arm description:

Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).

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

<b>Arm title</b>	Sodium Bicarbonate
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Arm description:

Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l), no treatment in run-in phase.

Arm type	Active comparator
Investigational medicinal product name	no intervention
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Other use

Dosage and administration details:

No intervention

Number of subjects in period 1	Control	Sodium Bicarbonate
Started	22	21
Completed	19	16
Not completed	3	5
Consent withdrawn by subject	3	5

**Period 2**

Period 2 title	Treatment phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

**Arms**

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Control

Arm description:

Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).

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

<b>Arm title</b>	Sodium Bicarbonate
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Arm description:

Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l) with the addition of oral sodium bicarbonate 500mg capsules for 12 weeks (weeks 5-16 of the study).

The dosage titrated to individual blood levels. Starting dose was 1g twice daily with the dose titrated during the first 4 weeks of treatment (increasing by 0.5g twice daily as tolerated, to a maximum of 3g bd) to achieve predialysis bicarbonate levels over 22mmols/L.

Arm type	Active comparator
Investigational medicinal product name	Sodium bicarbonate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Starting dose 1g bd (4 tablets per day) with the dose titrated during the first 4 weeks of treatment (increasing by 0.5g bd as tolerated, to a maximum 3g bd) to achieve predialysis bicarbonate over 22mmol/l.

<b>Number of subjects in period 2</b>	Control	Sodium Bicarbonate
Started	19	16
Completed	18	15
Not completed	1	1
Renal transplant	1	1

**Period 3**

Period 3 title	Wash out phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

**Arms**

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Control
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Arm description:

Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).

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

<b>Arm title</b>	Sodium Bicarbonate
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Arm description:

Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l), no treatment just follow-up

Arm type	Active comparator
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Investigational medicinal product name	no intervention
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule, hard
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Routes of administration	Other use
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Dosage and administration details:

no intervention

Number of subjects in period 3	Control	Sodium Bicarbonate
Started	18	15
Completed	18	15

## Baseline characteristics

### Reporting groups

Reporting group title	Control
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Reporting group description:

Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).

Reporting group title	Sodium Bicarbonate
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Reporting group description:

Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l), no treatment in run-in phase.

Reporting group values	Control	Sodium Bicarbonate	Total
Number of subjects	22	21	43
Age categorical			
Units: Subjects			
Adults (18-64 years)	14	13	27
From 65-84 years	8	8	16
Age continuous			
Units: years			
median	61	61	
standard deviation	± 9.7	± 14	-
Gender categorical			
Units: Subjects			
Female	5	5	10
Male	17	16	33
Haemodialysis vintage			
The time participants have been on haemodialysis			
Units: months			
median	38	32	
standard deviation	± 46	± 48	-

### Subject analysis sets

Subject analysis set title	Non-bic Control
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Measurements over the first 4 weeks (run-in phase) and last 4 weeks (wash out phase) to establish blood potassium profile.

Subject analysis set title	Non-bic Sodium Bicarbonate
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Measurements over the first 4 weeks (run-in phase) and last 4 weeks (wash out phase) to establish blood potassium profile.

Reporting group values	Non-bic Control	Non-bic Sodium Bicarbonate	
Number of subjects	19	15	

Age categorical			
Units: Subjects			
Adults (18-64 years)	14	13	
From 65-84 years	4	2	
Age continuous			
Units: years			
median	61	61	
standard deviation	$\pm 9.7$	$\pm 14$	
Gender categorical			
Units: Subjects			
Female	4	3	
Male	15	12	
Haemodialysis vintage			
The time participants have been on haemodialysis			
Units: months			
median	38	32	
standard deviation	$\pm 46$	$\pm 48$	



## End points

### End points reporting groups

Reporting group title	Control
Reporting group description: Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L(final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).	
Reporting group title	Sodium Bicarbonate
Reporting group description: Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l), no treatment in run-in phase.	
Reporting group title	Control
Reporting group description: Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L(final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).	
Reporting group title	Sodium Bicarbonate
Reporting group description: Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l) with the addition of oral sodium bicarbonate 500mg capsules for 12 weeks (weeks 5-16 of the study).  The dosage titrated to individual blood levels. Starting dose was 1g twice daily with the dose titrated during the first 4 weeks of treatment (increasing by 0.5g twice daily as tolerated, to a maximum of 3g bd) to achieve predialysis bicarbonate levels over 22mmols/L.	
Reporting group title	Control
Reporting group description: Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L(final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).	
Reporting group title	Sodium Bicarbonate
Reporting group description: Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l), no treatment just follow-up	
Subject analysis set title	Non-bic Control
Subject analysis set type	Sub-group analysis
Subject analysis set description: Measurements over the first 4 weeks (run-in phase) and last 4 weeks (wash out phase) to establish blood potassium profile.	
Subject analysis set title	Non-bic Sodium Bicarbonate
Subject analysis set type	Sub-group analysis
Subject analysis set description: Measurements over the first 4 weeks (run-in phase) and last 4 weeks (wash out phase) to establish blood potassium profile.	
<b>Primary: Inter-dialytic Change in Dialysis Potassium Level (Pre and Post Dialysis Potassium Level)</b>	
End point title	Inter-dialytic Change in Dialysis Potassium Level (Pre and Post Dialysis Potassium Level)
End point description:	
End point type	Primary
End point timeframe: 20 weeks	

<b>End point values</b>	Control	Sodium Bicarbonate	Non-bic Control	Non-bic Sodium Bicarbonate
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	19	15	19	15
Units: mmol/L				
geometric mean (standard deviation)	2.00 ( $\pm$ 0.63)	1.69 ( $\pm$ 0.49)	2.08 ( $\pm$ 0.64)	1.9 ( $\pm$ 0.60)

### Statistical analyses

<b>Statistical analysis title</b>	Change in Dialysis Potassium - Sodium Bicarbonate
Comparison groups	Sodium Bicarbonate v Non-bic Sodium Bicarbonate
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	paired t-test

<b>Statistical analysis title</b>	Change in Dialysis Potassium - Control
Comparison groups	Control v Non-bic Control
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	paired t-test

### Secondary: Changes in QT dispersion, 12 lead Electrocardiogram analysis

End point title	Changes in QT dispersion, 12 lead Electrocardiogram analysis
End point description:	
End point type	Secondary
End point timeframe:	
20 weeks	

End point values	Control	Sodium Bicarbonate	Non-bic Control	Non-bic Sodium Bicarbonate
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	19	15	19	15
Units: ms				
geometric mean (standard deviation)	8.8 (± 21.4)	10.4 (± 27.5)	8.7 (± 39.9)	8.8 (± 23)

## Statistical analyses

<b>Statistical analysis title</b>	Change in QT dispersion_control
Statistical analysis description:	
Control group	
Comparison groups	Control v Non-bic Control
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	paired t-test

<b>Statistical analysis title</b>	Change in QT dispersion Sodium bicarbonate
Comparison groups	Sodium Bicarbonate v Non-bic Sodium Bicarbonate
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.79
Method	paired t-test

## Secondary: Changes in Lean Tissue Mass

End point title	Changes in Lean Tissue Mass
End point description:	
Body composition measurement before dialysis with the validated body composition monitor by Fresenius to measure lean tissue mass	
Analysis of lean tissue mass between the start and end of the treatment phase of the study	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Control	Sodium Bicarbonate	Control	Sodium Bicarbonate
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	15	18	15
Units: percentage of lean mass				
arithmetic mean (standard deviation)	51.8 (± 13.7)	45.0 (± 12.2)	50.2 (± 12.1)	45.5 (± 12.5)

### Statistical analyses

<b>Statistical analysis title</b>	Changes in Lean Tissue Mass_Sodium Bicarbonate
Comparison groups	Sodium Bicarbonate v Sodium Bicarbonate
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	paired t-test

<b>Statistical analysis title</b>	Changes in Lean Tissue Mass Control
Comparison groups	Control v Control
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041
Method	paired t-test

### Secondary: Handgrip Strength

End point title	Handgrip Strength
End point description:	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	Control	Sodium Bicarbonate	Control	Sodium Bicarbonate
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	15	18	15
Units: kg				
arithmetic mean (full range (min-max))	31.2 (14 to 51)	26.6 (10 to 64)	29.7 (14.3 to 51.8)	26.2 (15.9 to 64.5)

### Statistical analyses

<b>Statistical analysis title</b>	Handgrip Strength Sodium Bicarbonate
Comparison groups	Sodium Bicarbonate v Sodium Bicarbonate
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.64
Method	paired t-test

<b>Statistical analysis title</b>	Handgrip Strength Control
Comparison groups	Control v Control
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.034
Method	paired t-test

### Secondary: Changes in Total Symptom Severity

End point title	Changes in Total Symptom Severity
End point description:	
End point type	Secondary
End point timeframe:	
20 weeks	

End point values	Control	Sodium Bicarbonate	Non-bic Control	Non-bic Sodium Bicarbonate
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	19	15	18	15
Units: score on scale				
arithmetic mean (standard deviation)	11.3 (± 7.4)	8.9 (± 6.6)	14.1 (± 9.6)	11.9 (± 9.2)

### Statistical analyses

<b>Statistical analysis title</b>	Total Symptom Severity Sodium Bicarbonate
Comparison groups	Sodium Bicarbonate v Non-bic Sodium Bicarbonate
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	paired t-test

<b>Statistical analysis title</b>	Copy of Total Symptom Severity Control
Comparison groups	Control v Non-bic Control
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	paired t-test

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

20 weeks

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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### Reporting groups

Reporting group title	Control
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Reporting group description:

Standard haemodialysis treatment thrice weekly using a standard dialysate containing bicarbonate at a concentration of 35mmols/L (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l).

Reporting group title	Sodium Bicarbonate
-----------------------	--------------------

Reporting group description:

Standard haemodialysis treatment thrice weekly, using a standard dialysate containing bicarbonate at a concentration of 35mmols/ (final dialysate bicarbonate 32mmol/l with acetate 3mmol/l), no treatment in run-in phase.

Serious adverse events	Control	Sodium Bicarbonate	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 22 (22.73%)	1 / 21 (4.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Cerebral infarct			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain bleed			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Rectus sheath haematoma			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Gallstone pancreatitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthralgia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Control	Sodium Bicarbonate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 22 (18.18%)	4 / 21 (19.05%)	
Cardiac disorders			
High blood pressure			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Gastrointestinal bleeding			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Diverticulitis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 21 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Enterococcus faecalis infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Chest infection			



subjects affected / exposed	0 / 22 (0.00%)	3 / 21 (14.29%)	
occurrences (all)	0	3	

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported