Clinical trial results:
A Direct obserVed therApy vs fortNightly CollEction Study for HCV Treatment – ADVANCE HCV Study

Summary

EudraCT number	2017-001039-38
Trial protocol	GB
Global end of trial date	28 October 2020

Results information

Result version number	v1 (current)
This version publication date	21 October 2021
First version publication date	21 October 2021
Summary attachment (see zip file)	ADVANCE trial summary (End of trial summary HRA.pdf)

Trial information

Trial identification

Sponsor protocol code	2016GA03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03236506
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor R&D number : 2016GA03

Notes:

Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	TASC, Ninewells Hospital, Level3, Dundee, United Kingdom, DD1 9SY
Public contact	Sarah Inglis, University of Dundee, Tayside Clinical Trials Unit, +44 01382383219, TASCgovernance@dundee.ac.uk
Scientific contact	Sarah Inglis, University of Dundee, Tayside Clinical Trials Unit, 1383383297 01382383219, TASCgovernance@dundee.ac.uk

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	20 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 October 2020
Global end of trial reached?	Yes
Global end of trial date	28 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to identify which one of three methods of treatment is the most effective in curing hepatitis C infection in people who inject drugs. The three methods we are testing are: 1. patients receiving their medication daily at their local pharmacy or needle exchange, 2. patients receiving their medication on a fortnightly basis from the needle exchange, 3. patients receiving their medication on a fortnightly basis from the needle exchange AND getting help from a psychologist to remember to take their medicine every day.

Protection of trial subjects:

Trial staff were trained to provide support if any participants became distressed during the trial visits.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2017
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 Kingdom: 135
Worldwide total number of subjects	135
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)	0
Adults (18-64 years)	135
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

135 people who inject drugs were recruited from injecting provision sites in Tayside, Scotland between January 2018 and November 2019

Pre-assignment

Screening details:

6 participants chose not to take after being consented. 129 were randomised.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Daily observed therapy

Arm description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a daily, observed basis by either the nurse or a community pharmacist.
Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection
Sofosbuvir Pill: Drugs will be given along with Zepatier to participants to treat genotype 3hepatitis C infection

Arm type	Experimental
Investigational medicinal product name	Zepatier
Investigational medicinal product code	EU/1/16/1119/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One daily for either 12 weeks (Genotype 1 HCV infection) or 8 weeks (Genotype 3 infection)

Investigational medicinal product name	Sovaldi
Investigational medicinal product code	EU/1/13/894/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One per day for 8 weeks (Genotype 3 HCV infection only)

Arm title	Fortnightly Pick-up

Arm description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse.
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Investigational medicinal product name	Sovaldi
Investigational medicinal product code	EU/1/13/894/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One per day for 8 weeks (Genotype 3 HCV infection only)

Arm title	Fortnightly Pick-up with Psych intervention

Arm description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse. In addition, this group will receive a one-off interview with the researcher to complete a psychological intervention designed to improve adherence to the medication regimen.
Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection
Psychological intervention: Participants randomised to fortnightly pick-up with psychological intervention will have an interview with the study nurse designed to aid their compliance with the drug regimen. During the intervention participants will be guided by their trial nurse in the completion of a personalised booklet, "Hepatitis C and Me". The booklet uses the principles of n

Arm type	Experimental
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Dosage and administration details:

One daily for either 12 weeks (Genotype 1 HCV infection) or 8 weeks (Genotype 3 infection)

Investigational medicinal product name	Sovaldi
Investigational medicinal product code	EU/1/13/894/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One per day for 8 weeks (Genotype 3 HCV infection only)

Number of subjects in period 1[1]	Daily observed therapy	Fortnightly Pick-up	Fortnightly Pick-up with Psych intervention
Started	39	42	47
Completed	33	37	40
Not completed	6	5	7
Adverse event, serious fatal	1	1	1
Consent withdrawn by subject	3	3	4

Protocol deviation	2	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 135 participants were consented to take part in the trial. 129 were randomised because 6 participants opted not to take part after consent. One individual who was randomised was ineligible and so not part of the analysis.

Baseline characteristics

Reporting groups	
Reporting group title	Daily observed therapy
Reporting group description:	
Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a daily, observed basis by either the nurse or a community pharmacist. Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection Sofosbuvir Pill: Drugs will be given along with Zepatier to participants to treat genotype 3hepatitis C infection	
Reporting group title	Fortnightly Pick-up
Reporting group description:	
Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse. Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection Sofosbuvir Pill: Drugs will be given along with Zepatier to participants to treat genotype 3hepatitis C infection	
Reporting group title	Fortnightly Pick-up with Psych intervention
Reporting group description:	
Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse. In addition, this group will receive a one-off interview with the researcher to complete a psychological intervention designed to improve adherence to the medication regimen. Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection Psychological intervention: Participants randomised to fortnightly pick-up with psychological intervention will have an interview with the study nurse designed to aid their compliance with the drug regimen. During the intervention participants will be guided by their trial nurse in the completion of a personalised booklet, "Hepatitis C and Me". The booklet uses the principles of n	

Reporting group values	Daily observed therapy	Fortnightly Pick-up	Fortnightly Pick-up with Psych intervention
Number of subjects	39	42	47
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	36.2	35.7	37.7
standard deviation	± 8.20	± 7.33	± 7.53

Gender categorical Units: Subjects			
Female	10	11	15
Male	29	31	32
Drug injecting history			
Participants asked whether they last injected illicit drugs during the last week, last month or last 3 months			
Units: Subjects			
Injected within last week	27	28	33
Injected within last month	4	8	6
Injected within last 3 months	8	6	8

Reporting group values	Total		
Number of subjects	128		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	36		
Male	92		
Drug injecting history			
Participants asked whether they last injected illicit drugs during the last week, last month or last 3 months			
Units: Subjects			
Injected within last week	88		
Injected within last month	18		
Injected within last 3 months	22		

End points

End points reporting groups

Reporting group title	Daily observed therapy

Reporting group description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a daily, observed basis by either the nurse or a community pharmacist.
Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection
Sofosbuvir Pill: Drugs will be given along with Zepatier to participants to treat genotype 3hepatitis C infection

Reporting group title	Fortnightly Pick-up

Reporting group description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse.
Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection
Sofosbuvir Pill: Drugs will be given along with Zepatier to participants to treat genotype 3hepatitis C infection

Reporting group title	Fortnightly Pick-up with Psych intervention

Reporting group description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse. In addition, this group will receive a one-off interview with the researcher to complete a psychological intervention designed to improve adherence to the medication regimen.
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Primary: Comparison of Sustained Viral Response at 12 Weeks Post Treatment (SVR12) in the Three Treatment Groups

End point title	Comparison of Sustained Viral Response at 12 Weeks Post Treatment (SVR12) in the Three Treatment Groups

End point description:

SVR12 was measured by PCR test to measure viral load of hepatitis c virus (HCV) in participant's blood at least 12 weeks after end of treatment. A viral load of less than 10IU/ml indicates no active infection and SVR12 has been achieved.

End point type	Primary

End point timeframe:

Measured at 12 weeks post end of treatment

End point values	Daily observed therapy	Fortnightly Pick-up	Fortnightly Pick-up with Psych intervention	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	37	40	
Units: Participants				
Positive for virus	3	5	3	
Negative for virus	30	32	37	

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Daily observed therapy v Fortnightly Pick-up
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.67
Method	logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	3

Notes:

[1] - Assuming a 95% SVR rate (based on published studies) in the DOT arm of the trial in this population and a non-inferiority limit of 14% (which would be likely to maintain cost-effectiveness) then at a 5% significance level and 90% power we would need a sample size of 42 in each group 126 in total. To allow for drop-outs we will aim to recruit 135 individuals, 45 per group

Statistical analysis title	Non-inferiority
Comparison groups	Fortnightly Pick-up v Fortnightly Pick-up with Psych intervention
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.41
Method	logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	2.45

Notes:

[2] - Assuming a 95% SVR rate (based on published studies) in the DOT arm of the trial in this population and a non-inferiority limit of 14% (which would be likely to maintain cost-effectiveness) then at a 5% significance level and 90% power we would need a sample size of 42 in each group 126 in total. To allow for drop-outs we will aim to recruit 135 individuals, 45 per group

Statistical analysis title	Non-inferiority
Comparison groups	Daily observed therapy v Fortnightly Pick-up with Psych intervention
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	= 0.82
Method	logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	6.61

Notes:

[3] - Assuming a 95% SVR rate (based on published studies) in the DOT arm of the trial in this population and a non-inferiority limit of 14% (which would be likely to maintain cost-effectiveness) then at a 5% significance level and 90% power we would need a sample size of 42 in each group 126 in total. To allow for drop-outs we will aim to recruit 135 individuals, 45 per group

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected for each participant while they were on the trial from consent until final data collection (SVR12). Trial contained active participants for a period of 31 months.

Adverse event reporting additional description:

Information about adverse events was collected when participants attended the injecting equipment provision sites for injecting equipment and followup.
Recorded but not reported as Serious Adverse Events:
Death or hospitalisation for assault or accidental injury
Hospitalisation for abscesses due to drugs use
Hospitalisation for wound management

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Daily observed therapy

Reporting group description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a daily, observed basis by either the nurse or a community pharmacist.
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Reporting group title	Fortnightly Pick-up

Reporting group description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse.
Zepatier Pill: Drugs will be given to participants to treat hepatitis C infection
Sofosbuvir Pill: Drugs will be given along with Zepatier to participants to treat genotype 3hepatitis C infection

Reporting group title	Fortnightly Pick-up with Psych intervention

Reporting group description:

Patients with active hepatitis C infection genotype 1 will receive 12 weeks treatment with Zepatier at one tablet per day. Patients with active hepatitis C infection genotype 3 will receive 8 weeks treatment with Zepatier pill plus Sofosbuvir pill at one of each tablets per day. These tablets will be given to patients on a fortnightly basis by the nurse. In addition, this group will receive a one-off interview with the researcher to complete a psychological intervention designed to improve adherence to the medication regimen.
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Serious adverse events	Daily observed therapy	Fortnightly Pick-up	Fortnightly Pick-up with Psych intervention
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 39 (15.38%)	9 / 42 (21.43%)	8 / 47 (17.02%)

number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Illicit drug overdose			
subjects affected / exposed	3 / 39 (7.69%)	1 / 42 (2.38%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Intentional self harm			
subjects affected / exposed	1 / 39 (2.56%)	0 / 42 (0.00%)	0 / 47 (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
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 39 (2.56%)	2 / 42 (4.76%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left mild cerebral infarct			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness due to drug use			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			

Physical assault			
subjects affected / exposed	1 / 39 (2.56%)	0 / 42 (0.00%)	0 / 47 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration pnuemonia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint swelling			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain secondary to fall			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Arthritis bacterial			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Community acquired pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abcess			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 42 (0.00%)	0 / 47 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic embolus			
subjects affected / exposed	0 / 39 (0.00%)	1 / 42 (2.38%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal bacteraemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 42 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Daily observed therapy	Fortnightly Pick-up	Fortnightly Pick-up with Psych intervention
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 39 (20.51%)	10 / 42 (23.81%)	6 / 47 (12.77%)
Injury, poisoning and procedural complications			
illicit drug overdose			
subjects affected / exposed	5 / 39 (12.82%)	0 / 42 (0.00%)	2 / 47 (4.26%)
occurrences (all)	5	0	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 39 (2.56%)	4 / 42 (9.52%)	1 / 47 (2.13%)
occurrences (all)	1	4	1
Reproductive system and breast disorders			
menorrhagia			
subjects affected / exposed	0 / 39 (0.00%)	3 / 42 (7.14%)	0 / 47 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Injection site infection/abscess			
subjects affected / exposed	2 / 39 (5.13%)	3 / 42 (7.14%)	3 / 47 (6.38%)
occurrences (all)	2	4	9

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31399460