Clinical trial results:
Telaprevir in patients with genotype 3 HCV : pilot clinical study to evaluate efficacy and predictability of therapy in patients who have failed to respond to pegylated interferon and ribavirin

Summary

EudraCT number	2013-003729-27
Trial protocol	GB
Global end of trial date	02 November 2017

Results information

Result version number	v1 (current)
This version publication date	09 December 2017
First version publication date	09 December 2017
Summary attachment (see zip file)	TIG3 summary (TIG3 report - summary PDF.pdf)

Trial information

Trial identification

Sponsor protocol code	0.8

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02087111
WHO universal trial number (UTN)	-
Other trial identifiers	Graham Foster: PI

Notes:

Sponsors

Sponsor organisation name	Queen Mary University of London
Sponsor organisation address	5 Walden Street, London, United Kingdom, E1 2EF
Public contact	Foster, Queen Marys School of Medicine, 0044 0207 882 7242, g.r.foster@qmul.ac.uk
Scientific contact	Foster, Queen Marys School of Medicine, 0044 207 882 7242, g.r.foster@qmul.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	02 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2017
Global end of trial reached?	Yes
Global end of trial date	02 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Do patients with genotype 3 hepatitis C and cirrhosis who have failed to respond to pegylated interferon and ribavirin respond to retreatment with pegylated interferon, ribavirin and telaprevir?
Does pre-treatment viral phenotyping identify patients who respond to pegylated interferon, ribavirin and telaprevir?

Protection of trial subjects:

An independent monitoring committee monitored the study and reviewed patient safety

Background therapy:

The patient population studied (Genotype 3 with cirrhosis who had failed standard therapy) had no treatment options available and therefore there was no comparator or background therapy

Evidence for comparator:

Not required, there was no comparator

Actual start date of recruitment	03 June 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	14
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment from 4 July 2014 to 6 November 2014. Recruitment took place in four English centres - Barts Health, London, St Georges Hospital, London, Bradford Royal Infirmary and Nottingham University Hospital

Pre-assignment

Screening details:

Patients with genotype 3 HCV and cirrhosis who had failed to respond to therapy with pegylated interferon and ribavirin were screened for the study.

Pre-assignment period milestones

Number of subjects started	14
Number of subjects completed	14

Period 1

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

Arms

Arm title	Active arm

Arm description:

Active arm

Arm type	Experimental
Investigational medicinal product name	Pegasys (Pegylated interferon-alfa 2a)
Investigational medicinal product code	ATC code = L03AB11
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

180 micrograms once a week given as a subcutaneous injection

Investigational medicinal product name	Ribavirin (Copegus)
Investigational medicinal product code	ATC code = J05AB04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg administered twice a day, total dose 800mg

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	MA code EU/1/11/720/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1125mg administered twice a day

Number of subjects in period 1	Active arm
Started	14
Completed	14

Period 2	
Period 2 title	Post 4 week therapy
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Active arm

Arm description:

Active arm

Arm type	Experimental
Investigational medicinal product name	Pegasys (Pegylated interferon-alfa 2a)
Investigational medicinal product code	ATC code = L03AB11
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

180 micrograms once a week given as a subcutaneous injection

Investigational medicinal product name	Ribavirin (Copegus)
Investigational medicinal product code	ATC code = J05AB04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg administered twice a day, total dose 800mg

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	MA code EU/1/11/720/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1125mg administered twice a day

Number of subjects in period 2	Active arm
Started	14
Completed	10
Not completed	4
Consent withdrawn by subject	1
Lack of efficacy	3

Period 3	
Period 3 title	End of therapy
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Active arm
Arm description: Active arm	
Arm type	Experimental
Investigational medicinal product name	Pegasys (Pegylated interferon-alfa 2a)
Investigational medicinal product code	ATC code = L03AB11
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details: 180 micrograms once a week given as a subcutaneous injection	
Investigational medicinal product name	Ribavirin (Copegus)
Investigational medicinal product code	ATC code = J05AB04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 400 mg administered twice a day, total dose 800mg	
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	MA code EU/1/11/720/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1125mg administered twice a day	

Number of subjects in period 3	Active arm
Started	10
Completed	9
Not completed	1
Lack of efficacy	1

Period 4	
Period 4 title	SVR
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Active arm

Arm description:

Active arm

Arm type	Experimental
Investigational medicinal product name	Pegasys (Pegylated interferon-alfa 2a)
Investigational medicinal product code	ATC code = L03AB11
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

180 micrograms once a week given as a subcutaneous injection

Investigational medicinal product name	Ribavirin (Copegus)
Investigational medicinal product code	ATC code = J05AB04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg administered twice a day, total dose 800mg

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	MA code EU/1/11/720/001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1125mg administered twice a day

Number of subjects in period 4	Active arm
Started	9
Completed	9

Baseline characteristics

Reporting groups	
Reporting group title	Active arm
Reporting group description:	
Active arm	

Reporting group values	Active arm	Total	
Number of subjects	14	14	
Age categorical			
Characteristics of patients			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	14	14	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	47		
full range (min-max)	32 to 63	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	10	10	
Ethnic group			
Ethnicity			
Units: Subjects			
Caucasian	6	6	
Asian	7	7	
Other	1	1	

End points

End points reporting groups

Reporting group title	Active arm
Reporting group description: Active arm	
Reporting group title	Active arm
Reporting group description: Active arm	
Reporting group title	Active arm
Reporting group description: Active arm	
Reporting group title	Active arm
Reporting group description: Active arm	
Subject analysis set title	SVR rate
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients who achieved a sustained virological response	

Primary: Sustained virological response

End point title	Sustained virological response[1]
End point description: Sustained virological response	
End point type	Primary
End point timeframe: Post therapy	

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: The trial was discontinued before an adequate number of patients had been recruited. The trial was terminated because new drugs had been licensed rendering this therapy inappropriate. The steering committee deemed it unethical to continue the trial. Analysis of 14 patients is clearly inappropriate

End point values	Active arm			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Individuals				
SVR	4			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Virological response after 4 weeks

End point title	Virological response after 4 weeks
End point description: Number responding after 4 weeks	

End point type	Other pre-specified

End point timeframe:

4 weeks after therapy initiated

End point values	Active arm			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Individuals				
EVR	10			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: End of therapy response

End point title	End of therapy response

End point description:

End of therapy response

End point type	Other pre-specified

End point timeframe:

End of therapy

End point values	Active arm			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Individuals				
ETR	9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Trial commencement until completion of results analysis - specifically 2 June 2013 to 8 September 2017

Adverse event reporting additional description:

All patients developed at least one adverse event.

Assessment type	Non-systematic

Dictionary used

Dictionary name	SNOMED CT
Dictionary version	1.36.4

Reporting groups

Reporting group title	Treatment arm

Reporting group description:

Contains all patients in the trial

Serious adverse events	Treatment arm		
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	Treatment arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
Nervous system disorders			
Insomnia			
subjects affected / exposed	6 / 14 (42.86%)		
occurrences (all)	6		
Dizzyness			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	4		
Paresthesiae			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		

Memory impairment subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Visual disturbance subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2		
Dysguesia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2		
Headache subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	7 / 14 (50.00%) 7		
Pyrexia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 4		
Blood and lymphatic system disorders Thrombocytopaenia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Anaemia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Gastrointestinal disorders Proctalgia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Nausea alternative assessment type: Systematic			

subjects affected / exposed	9 / 14 (64.29%)		
occurrences (all)	10		
Vomiting			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Loss of appetite			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Dyspepsia			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Rectal bleeding			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Dental abscess			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Sore mouth			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Vaginal discomfort			

subjects affected / exposed[1]	1 / 4 (25.00%)		
occurrences (all)	1		
Vaginal candidiasis			
subjects affected / exposed[2]	1 / 4 (25.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences (all)	5		
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hepatobiliary disorders			
Elevated GGT			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Elevated bilirubin			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	11 / 14 (78.57%)		
occurrences (all)	21		
Pruritis			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences (all)	5		
Periorbital oedema			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hair loss			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Psychiatric disorders			

Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Weakness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Anxiety disorder			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Generalised pain			
subjects affected / exposed	5 / 14 (35.71%)		
occurrences (all)	5		
Lower limb pain			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Foot injury			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Only women or transgenders are capable of suffering vaginal symptoms

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Only women or transgenders are capable of suffering vaginal symptoms

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

During the trial an alternative treatment option for these patients was licensed and made available by NHSE and given the superiority of the newly licensed therapy it was deemed unethical to continue the study which was therefore stopped prematurely

Notes: