# Clinical trial results:
# An open label, randomised, pilot trial of pegylated interferon, ribavirin and telaprevir versus pegylated interferon and ribavirin alone in the response guided treatment of acute hepatitis C genotype 1 virus infection in patients with HIV-1 co-infection

## Summary

| | |
|---|---|
| EudraCT number | 2012-005525-75 |
| Trial protocol | GB |
| Global end of trial date | 29 February 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 16 November 2017 |
| First version publication date | 16 November 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | SSAT052 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02006745 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | St Stephens Aids Trust |
| Sponsor organisation address | Chelsea Chambers, 262a Fulham Road, London, United Kingdom, SW10 9NH |
| Public contact | Marita Marshall, Head of Project Management, St Stephen's Clinical Research, +44 0203 828 0567, marita.marshall@ststcr.com |
| Scientific contact | Prof Mark Nelson, St Stephan’s Centre, Chelsea & Westminster Hospital, +44 0203 315 5610 , mark.nelson@chelwest.nhs.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 | 14 April 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 February 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 February 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To find out whether treating acute hepatitis C infection with PEGylated interferon, ribavirin and telaprevir gets rid of the virus as effectively as when acute hepatitis C infection is treated with PEGylated interferon and ribavirin alone

Protection of trial subjects:

The protocol was written, and the study was conducted according to ICH GCP & the principles of the Declaration of Helsinki. The protocol was approved by the National Regulator & an Independent Ethics Committee as required by national legislation.

Written informed consent was obtained from each subject prior to evaluations being performed for eligibility.
The inclusion/exclusion criteria were designed to eliminate subjects who may have been put at risk by participating in the study. Safety & tolerability of medications were assessed by questions, physical examination & laboratory parameters. Any changes in health status during the study were recorded and followed up by the clinical team.

Female patients of childbearing potential & their male partners were required to use 2 effective contraceptive methods during treatment (as agreed by the investigator including a barrier method of contraception) and for at least 6 months after the last treatment (i.e. 6 months after week 12, 24 or 48, depending on study arm and treatment response). Routine monthly pregnancy tests were also required during this time and for 6 months after the end of treatment.

Heterosexually active male participants or their female partners were required to use 2 effective contraceptive methods during the trial and for at least 7 months after the last dosage of treatment.

Glucose monitoring was added to study procedures in line with information arising in an update to the SPC for Pegasys® during the study.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 13 May 2013 |
| 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: 24 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 24 |

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) | 24 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

20 adult male & female HIV-1 positive patients with current documented acute hepatitis C genotype 1 infection with an estimated duration of <24 weeks at diagnosis, were recruited from the out-patient clinics at Chelsea & Westminster Hospital NHS Foundation Trust between 21/01//2014 & 20/10/2016.

### Pre-assignment

Screening details:

24 patients were screened. There were a total of 6 screen failures. 2 of the screen failures underwent a second screening and were recruited to the study. Following successful screening, eligible patients were randomised at the baseline visit to treatment arm 1 or 2 in a 1:1 ratio.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 24 |
| Number of subjects completed | 20 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | Protocol deviation: 4 |

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm 1 |

Arm description:

PEG-IFN and weight-based ribavirin (RBV): 24 weeks in those achieving rapid virologic response (RVR (>2 log drop within 100 days of infection)) (undetectable HCV RNA at 4 weeks) or 48 weeks in those not achieving RVR

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | J05AB04 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1000 – 1200 mg daily (body mass-dependent) in two divided doses, to be taken orally

| | |
|---|---|
| Investigational medicinal product name | PEG-IFN |
| Investigational medicinal product code | L03AB11 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

180mcg once weekly

| | |
|---|---|
| **Arm title** | Arm 2 |

Arm description:

PEG-IFN and weight-based RBV plus telaprevir (TPV): 12 weeks in those achieving RVR, 24 weeks in

those not achieving RVR (HCV RNA >25 but <1000 iU/mL at week 4) or 48 weeks in those not achieving RVR (HCV RNA >1000 iU/mL at week 4) Patients achieving HCV RNA <25 iU/mL at week 4 (RVR) were treated for 12 weeks. Patients with HCV RNA above 25 but below 1000 iU/mL at week 4 were treated for 24 weeks (12 weeks of TPV/Peg-IFN/RBV followed by 12 weeks of Peg-IFN/RBV). Patients in arm 2 with HCV RNA > 1000 iU/mL at week 4 discontinued Telaprevir, continuing with PEG-IFN/RBV for an additional 44 weeks beyond week 4.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | PEG-IFN |
| Investigational medicinal product code | L03AB11 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

180mcg once weekly

| | |
|---|---|
| Investigational medicinal product name | telaprevir |
| Investigational medicinal product code | J05AE11 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

2x 375mg tablets q8hrly or 3x375mg tablets BID

| | |
|---|---|
| Investigational medicinal product name | Ribavirin |
| Investigational medicinal product code | J05AB04 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1000 – 1200 mg daily (body mass-dependent) in two divided doses, to be taken orally

| **Number of subjects in period 1[1]** | Arm 1 | Arm 2 |
|---|---|---|
| Started | 10 | 10 |
| Completed | 10 | 9 |
| Not completed | 0 | 1 |
| Lost to follow-up | - | 1 |

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: 4 subjects failed the screening period and so were not included in the baseline period

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Arm 1 |
| Reporting group description: | |
| PEG-IFN and weight-based ribavirin (RBV): 24 weeks in those achieving rapid virologic response (RVR (>2 log drop within 100 days of infection)) (undetectable HCV RNA at 4 weeks) or 48 weeks in those not achieving RVR | |
| Reporting group title | Arm 2 |
| Reporting group description: | |
| PEG-IFN and weight-based RBV plus telaprevir (TPV): 12 weeks in those achieving RVR, 24 weeks in those not achieving RVR (HCV RNA >25 but <1000 iU/mL at week 4) or 48 weeks in those not achieving RVR (HCV RNA >1000 iU/mL at week 4) Patients achieving HCV RNA <25 iU/mL at week 4 (RVR) were treated for 12 weeks. Patients with HCV RNA above 25 but below 1000 iU/mL at week 4 were treated for 24 weeks (12 weeks of TPV/Peg-IFN/RBV followed by 12 weeks of Peg-IFN/RBV). Patients in arm 2 with HCV RNA > 1000 iU/mL at week 4 discontinued Telaprevir, continuing with PEG-IFN/RBV for an additional 44 weeks beyond week 4. | |

| Reporting group values | Arm 1 | Arm 2 | Total |
|---|---|---|---|
| Number of subjects | 10 | 10 | 20 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 10 | 10 | 20 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| median | 38.7 | 39.2 | |
| full range (min-max) | 26.9 to 58.7 | 31.6 to 49.7 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 10 | 10 | 20 |
| Self Described Ethnicity<br>Units: Subjects | | | |
| English/Welsh/Scottish/Northern Irish/British | 3 | 3 | 6 |
| Irish | 1 | 1 | 2 |
| Any other white background | 4 | 5 | 9 |
| Chinese | 1 | 0 | 1 |
| African | 0 | 1 | 1 |
| Caribbean | 1 | 0 | 1 |

## End points

### End points reporting groups

| Reporting group title | Arm 1 |
|---|---|

Reporting group description:

PEG-IFN and weight-based ribavirin (RBV): 24 weeks in those achieving rapid virologic response (RVR (>2 log drop within 100 days of infection)) (undetectable HCV RNA at 4 weeks) or 48 weeks in those not achieving RVR

| Reporting group title | Arm 2 |
|---|---|

Reporting group description:

PEG-IFN and weight-based RBV plus telaprevir (TPV): 12 weeks in those achieving RVR, 24 weeks in those not achieving RVR (HCV RNA >25 but <1000 iU/mL at week 4) or 48 weeks in those not achieving RVR (HCV RNA >1000 iU/mL at week 4) Patients achieving HCV RNA <25 iU/mL at week 4 (RVR) were treated for 12 weeks. Patients with HCV RNA above 25 but below 1000 iU/mL at week 4 were treated for 24 weeks (12 weeks of TPV/Peg-IFN/RBV followed by 12 weeks of Peg-IFN/RBV). Patients in arm 2 with HCV RNA > 1000 iU/mL at week 4 discontinued Telaprevir, continuing with PEG-IFN/RBV for an additional 44 weeks beyond week 4.

### Primary: Comparison of rates of sustained virologic response (SVR24) between treatment arms; defined as HCV RNA not detectable at 24 weeks after planned completion of therapy.

| End point title | Comparison of rates of sustained virologic response (SVR24) between treatment arms; defined as HCV RNA not detectable at 24 weeks after planned completion of therapy.[1] |
|---|---|

End point description:

Comparison of SVR between arms by intention to treat analysis. Last observation HepC PCR <1000 iU/mL carried forward if data unavailable at a visit day. Where success is defined as any patient who achieves HepC PCR <1000 iU/mLn at a study visit time point and these results are assumed and retained for subsequent visits

| End point type | Primary |
|---|---|

End point timeframe:

24 weeks after planned completion of 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: Descriptive statistics only performed

| End point values | Arm 1 | Arm 2 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 10 | | |
| Units: Subjects | | | | |
| <1000 iU/mL | 9 | 10 | | |
| >1000 iU/mL | 1 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Comparison of proportion of treated patients achieving sustained virological response after 12 weeks of therapy (SVR12) between treatment arms;

| defined as HCV RNA not detected at 12 weeks after planned completion of therapy | |
|---|---|
| End point title | Comparison of proportion of treated patients achieving sustained virological response after 12 weeks of therapy (SVR12) between treatment arms; defined as HCV RNA not detected at 12 weeks after planned completion of therapy |

End point description:

Comparison of the parameters between arms by intention to treat analysis. . Last observation HepC PCR <1000 iU/mL carried forward if data unavailable at a visit day. Where success is defined as any patient who achieves HepC PCR <1000 iU/mL at a study visit time point and these results are assumed and retained for subsequent visits

| End point type | Secondary |
|---|---|

End point timeframe:

12 weeks after planned completion of therapy

| End point values | Arm 1 | Arm 2 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 10 | | |
| Units: Subjects | | | | |
| <1000 iU/mL | 9 | 10 | | |
| >1000 iU/mL | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

| Secondary: Comparison of proportion of treated patients with HCV RNA not detected at the planned end of treatment (EOT) between treatment arms | |
|---|---|
| End point title | Comparison of proportion of treated patients with HCV RNA not detected at the planned end of treatment (EOT) between treatment arms |

End point description:

Comparison of the parameters between arms by intention to treat analysis.

| End point type | Secondary |
|---|---|

End point timeframe:

Baselines to 48 weeks

| End point values | Arm 1 | Arm 2 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 10 | | |
| Units: # Subjects with HCV RNA PCR <1000 iU/mL | | | | |
| Baseline | 0 | 1 | | |
| 12 weeks | 9 | 10 | | |
| 24 weeks | 9 | 10 | | |
| 48 weeks | 9 | 10 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Comparison of reduction in HCV RNA from baseline to week 4 between treatment arms

| End point title | Comparison of reduction in HCV RNA from baseline to week 4 between treatment arms |
|---|---|

End point description:

Comparison of the parameters between arms by intention to treat analysis.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to week 4

| End point values | Arm 1 | Arm 2 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 10 | | |
| Units: # Subjects with HCV RNA PCR <1000 iU/mL | | | | |
| Baseline | 0 | 1 | | |
| Week 4 | 4 | 7 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Comparison of change in CD4 cell count between baseline and EOT between treatment arms

| End point title | Comparison of change in CD4 cell count between baseline and EOT between treatment arms |
|---|---|

End point description:

Comparison of the parameters between arms by intention to treat analysis.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline to End of Treatment

| End point values | Arm 1 | Arm 2 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 10 | | |
| Units: CD4 % | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Post Week 4 | 36.85 (27.80 to 41.50) | 42.35 (38.65 to 43.60) | | |
| Post Week 12 | 33.25 (31.10 to 36.20) | 37.40 (36.20 to 39.30) | | |
| Post week 24 | 36.75 (30.6 to 39.6) | 34.90 (32.05 to 40.65) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Summary comparison of adverse events of grade III / IV intensity between treatment arms

| End point title | Summary comparison of adverse events of grade III / IV intensity between treatment arms |
|---|---|

End point description:

Comparison of the parameters between arms by intention to treat analysis.

| End point type | Secondary |
|---|---|

End point timeframe:

Adverse events were captured from the point of consent to the end of study participation for each subject

| End point values | Arm 1 | Arm 2 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 10 | | |
| Units: Subjects | | | | |
| Baseline | 1 | 0 | | |
| Week 24 | 1 | 1 | | |
| Week 36 | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Adherence to medication (as measured by adherence questioning and pill counts)

| End point title | Adherence to medication (as measured by adherence questioning and pill counts) |
|---|---|

End point description:

Comparison of the parameter between arms by intention to treat analysis

| End point type | Secondary |
|---|---|

End point timeframe:

Compliance was measured during the treatment phases of the study

| **End point values** | Arm 1 | Arm 2 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 10 | | |
| Units: # Non Compliant Subjects | | | | |
| Week 2 | 0 | 1 | | |
| Week 4 | 3 | 1 | | |
| Week 8 | 2 | 1 | | |
| Week 12 | 1 | 2 | | |
| Week 24 | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From consent to Last visit for each patient | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Arm 1 |
| Reporting group description: - | |
| Reporting group title | Arm 2 |
| Reporting group description: - | |

| Serious adverse events | Arm 1 | Arm 2 | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 10 (10.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Gastrointestinal disorders | | | |
| RUPTURED COLON | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Arm 1 | Arm 2 | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | 10 / 10 (100.00%) | |
| Surgical and medical procedures | | | |
| Dental Extraction | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 10 (90.00%) | 7 / 10 (70.00%) | |
| occurrences (all) | 9 | 7 | |
| Febrile illness | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Flu like illness | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 3 / 10 (30.00%) | |
| occurrences (all) | 0 | 3 | |
| Flu like symptoms | | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Lethargy | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 10 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| Loss of appetite | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Low appetite | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Shiver | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tiredness | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 3 / 10 (30.00%) | |
| occurrences (all) | 0 | 3 | |
| Tiredness / 1 episode of synope | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| Cough | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dry Skin | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 2 / 10 (20.00%) | |
| occurrences (all) | 1 | 2 | |
| Hayfever | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 1 | 1 | |
| Sore Throat | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Reproductive system and breast disorders | | | |
| Erectile Dysfunction | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| SUPERFICIAL THROMBOPHLEBITIS (DORSAL PENILE VEINS) | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Viral URTI | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| EPITAXIS | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Left side chest discomfort | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 1 | 1 | |
| Shortness of breath on exertion | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 4 / 10 (40.00%) | |
| occurrences (all) | 0 | 4 | |
| LOW MOOD | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Mood swings | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Sleep disturbances | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Worsening anxiety | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Worsening Insomnia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 2 / 10 (20.00%) | |
| occurrences (all) | 2 | 2 | |
| Lack of concentration | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Syncope | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood and lymphatic system disorders | | | |
| low hemoglobin | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Acute gastroenteritis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | | |
|---|---|---|---|---|
| Anaemia | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 0 | 1 | | |
| COLOSTOMY | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 0 | 1 | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 4 / 10 (40.00%) | | |
| occurrences (all) | 2 | 4 | | |
| Diffuse itchiness | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 0 | 1 | | |
| Doxycycline related nausea | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Dry Cough | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 0 | 1 | | |
| E. Coli UTI | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Early Satiety | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 0 | 1 | | |
| Frequency stool | | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 0 | 1 | | |
| Gastroenteritis acute | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Heartburn | | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | 1 | | |
| Loose stool | | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 1 / 10 (10.00%) | | |
| occurrences (all) | 2 | 1 | | |

| | | | |
|---|---|---|---|
| Nausea | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 4 / 10 (40.00%) | |
| occurrences (all) | 0 | 4 | |
| Oesophageal reflux | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Post surgical bowel occlusion | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Shigellosis | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Soft stool | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Stomach Cramp | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Aplithris mouth ulcer | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Arthralgia knee | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Dermatitis oricomieosis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dry thickened skin both ankles | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Itch | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Itchy rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Itchy skin | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 3 / 10 (30.00%) | |
| occurrences (all) | 0 | 3 | |
| Middle finger L. hand itching swelling | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mosquito bites | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mouth ulcer | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Night sweats | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 1 | 1 | |
| Pruritis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Rash | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 2 | 1 | |
| Red spot on face | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| SKIN SCALP INFECTION | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Skin tag removal | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Wasp sting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Worsening proteinuria (renoprotective) | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Aches and pains | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Acne/Back + neck | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Bone aches Pain | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Left hip burisitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Left upper arm bruise. Mechanical fall | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Mild discomfort right flank | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Myalgia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| right 3RD metacarphalagial joint pain | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Right knee pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Anal Gonorhoea | | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Angular cheilitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Anxiety (worsening) | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Chlamydia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dental Abscess | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dental infection | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Herpatic lip ulcer | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Onychomycose left toe nail | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Peritonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Secondary syphilis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Syphilis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 10 October 2013 | This amendment was generated in order to clarify points raised by the ethics committee in their letter dated 16th July 2013, and to add that viral load plasma samples will be stored for possible further testing. |
| 07 January 2014 | Addition of fibroscans, clarify the study follow up visits, remove the hepatitis C risk factors questionnaire, increase the volume of blood taken for stored samples and update the dosing information, as well as to make a number of administrative changes. |
| 01 September 2014 | Updated in line with new safety information from Pegasys® SPC. Addition of glucose testing and Hep-B Testing. Updated contraception advice |
| 26 November 2015 | Data to be combined with that from a similar study (An open label, randomised, non-inferiority trial of pegylated interferon, ribavirin and telaprevir versus pegylated interferon and ribavirin alone in the response guided treatment of acute hepatitis C genotype 1 virus infection in patients with HIV-1 co-infection (CHAT Study) ) which was being concurrently carried out by the University of Bonn, Germany. The PIs from the 2 studies were to lead the combined analysis. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported