ISRCTN64847145 https://doi.org/10.1186/ISRCTN64847145

Exploring the effect of disturbance in insulin metabolism on the treatment response of hepatitis C virus to find options to improve response rate

Submission date 07/12/2009	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 15/01/2010	**Overall study status** Stopped	
Last Edited 03/09/2014	**Condition category** Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2009-016678-34

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EudraCT No: 2009-016678-34

Study information

Scientific Title
Exploring the relationship between insulin resistance and interferon resistance: options to overcome Hepatitis C Virus (HCV) non-response to pegylated interferon

Study objectives
Hepatitis C virus (HCV) infection is a serious problem. Currently, pegylated interferon and ribavirin treatment can result in cure. However, the average overall cure rate is about 55% of patients. This average depends on the viral genotypes (substrains). For example, the cure rate is lower in HCV genotype 1 and 4 than HCV genotype 2 and 3. In addition, patients with liver cirrhosis (scarring) have a lower chance to respond to treatment. Furthermore, there is new scientific evidence that disturbance in insulin metabolism, which is called insulin resistance, may lower the treatment response. Insulin resistance can be caused by obesity and/or diabetes mellitus (DM). Now, there is new evidence that HCV per se can cause insulin resistance. This means that any patient with HCV infection could have insulin resistance even if he/she is non-obese and non-diabetic. As insulin resistance can decrease the chance of cure in response to current treatment, so improving insulin resistance may improve the treatment response and overall cure rate. Insulin resistance can be improved by pioglitazone oral tablets treatment which is currently used for patients with DM.
The objective of this study is to improve the overall cure rate in response to treatment by pegylated interferon and ribavirin by addition of pioglitazone to improve insulin resistance.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical approval is in progress. Within December 2010, will apply to:
1. Medicines and Healthcare products Regulatory Agency (MHRA)
2. NHS/Health and Social Care (HSC) R&D office
3. Social Care Research Ethics Committee
4. NHS Ssci

Study design
Prospective open-label study

Primary study design
Interventional

Secondary study design
Other

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Hepatitis C Virus (HCV) infection

Interventions
In stage 1, we will investigate the physiologic response to pioglitazone therapy by comparing measured total insulin resistance, hepatic insulin resistance, interferon sensitivity and virologic response before and after a 12-week course of pioglitazone.
The total duration of follow-up for stage I will be 13 weeks.

In stage 2, pioglitazone 30 mg will be added to standard therapy for two groups of patients: a) group I consisted of naïve patients with HCV genotype 1 infection and b) group II consisted of patients with hepatitis C and compensated liver cirrhosis (Ishak fibrosis score ≥5) who failed to respond to previous treatment. The impact of adding pioglitazone to standard treatment on sustained virologic response (SVR) will be determined after a full course of pegylated interferon and ribavirin treatment in addition to pioglitazone therapy.
The total duration of follow-up for stage II will be 1.5 years.

Updated 03/09/2014: the trial was stopped in 2011 due to poor recruitment.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Insulin resistance:
Total body insulin resistance and hepatic insulin resistance will be measured using the hyperinsulinaemic euglycaemic clamp.

Secondary outcome measures
1. Interferon sensitivity (Interferon-Inducible Protein [IP10] in blood measured by ELISA and in peripheral blood mononuclear cells [PBMC] by mRNA)
2. Viral dynamic response measured by serial HCV PCR levels
3. Treatment response measured by serial HCV PCR levels

Overall study start date
01/02/2010

Completion date
31/01/2012

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Chronic HCV genotype 1 infection
2. Chronic HCV and compensated liver cirrhosis who failed to respond to previous treatment
3. Age >17, <70
4. Eligible for interferon therapy

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
22 patients

Key exclusion criteria
1. HIV or HBV co-infection
2. Current use antidiabetic medication (e.g., insulin, metformin or thiazolidinedione)
3. Significant respiratory, cardiac or renal dysfunction
4. Body Mass Index > 30 kg/m2

Date of first enrolment
01/02/2010

Date of final enrolment
31/01/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Hepatology Section
London
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Sponsor information

Organisation
Imperial College London and Imperial College Healthcare NHS Trust (UK)

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Sponsor type
University/education

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Funder(s)

Funder type
University/education

Funder Name
Imperial College London (UK) - Hepatology Section

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration