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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

Registration date
15/01/2010

Last Edited
03/09/2014

Recruitment status
Stopped

Overall study status
Stopped

Condition category
Infections and Infestations

[X] Prospectively registered

[_] Protocol

[_] Statistical analysis plan

[_] Results

[_] Individual participant data

[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2009-016678-34

Protocol serial number

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

Study type(s)
Treatment

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(s)
Insulin resistance:
Total body insulin resistance and hepatic insulin resistance will be measured using the hyperinsulinaemic euglycaemic clamp.

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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
United Kingdom

England

Study participating centre
Hepatology Section
London
United Kingdom
W2 1NY

Sponsor information

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

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
University/education

Funder Name

Imperial College London (UK) - Hepatology Section

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration