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Consecutive blood letting and peginterferon alfa-2a/ribavirin standard treatment compared to peginterferon alfa-2a/ribavirin standard treatment alone for naive patients with hepatitis C virus genotype one and elevated ferritin levels

Submission date	Recruitment status	[_] Prospectively registered
26/06/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/08/2006	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/01/2021	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

Protocol serial number
ML 20073 Version 4.2

Study information

Scientific Title
Consecutive blood letting and peginterferon alfa-2a/ribavirin standard treatment compared to peginterferon alfa-2a/ribavirin standard treatment alone for naive patients with hepatitis C virus genotype one and elevated ferritin levels

Acronym
KAPRI

Study objectives
This is a randomised phase IV study of blood letting in combination with the peginterferon alfa-2a/ribavirin standard treatment in Hepatitis C Virus (HCV) positive patients with an elevated level of ferritin.

Blood letting (the removal of 400-500 ml blood) will be carried out before the start of the antiviral treatment at weekly intervals until a target ferritin level of more than or equal to 50-100 µg/l is reached. If the haemoglobin drops by less than or equal to 12 g/d in men or less than or equal to 11 g/d in women, the blood letting treatment will be stopped without reaching the target ferritin. No further treatment will then be planned for these patients within the framework of this clinical trial. Patients who reach a target ferritin level of more than or equal to 50 to less than or equal to 100 µg/l will then receive further to the blood letting a combination treatment of peginterferon alfa-2a and ribavirin for 48 weeks.

The primary aim of this study will be a determination of the virus kinetics in the first 12 weeks of the peginterferon alfa-2a/ribavirin combination treatment in patients who have received the blood letting treatment compared with patients who have not received the blood letting treatment. Secondary aims will include the efficacy of the added treatment, the improvement of serum fibrosis markers, early and normal virological response and the safety and compatibility of blood letting treatment with the peginterferon alfa-2a/ribavirin standard treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Commission of the Medical Faculty of Heinrich Heine University Hospital, Dusseldorf (reference number MC-LKP-105) dated 30/05/2006.

Study design
Multicentric, randomised, prospective open phase IV study in a parallel group design

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Arm A: blood letting (phlebotomy) treatment until the required target ferritin level is reached (Ferritin more than or equal to 50 µg/l to less than or equal to 100 µg/l) but only until a maximum of 24 weeks is reached. Then standard treatment of 180 µg peginterferon alfa-2a once a week and 1000-1200 mg ribavirin daily for 48 weeks.
Arm B: standard treatment of 180 µg peginterferon alfa-2a once a week and 1000-1200 mg ribavirin daily for 48 weeks.

The treatment of both arms will be followed by a follow-up monitoring phase of 24 weeks without treatment.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Ribavirin and peginterferon alfa-2a

Primary outcome(s)
Determination of the virus kinetics in the first 12 weeks of peginterferon alfa-2a/ribavirin combination treatment in patients with elevated levels of ferritin and previous blood letting treatment (Arm A) compared to peginterferon alfa-2a/ribavirin combination treatment in patients with elevated ferritin levels without previous blood letting treatment (Arm B).

Key secondary outcome(s))
1. Comparison of the efficacy (defined as Sustained Virological Response [SVR]) 24 weeks after the end of treatment
2. Improvement of serum fibrosis markers
3. Virological response at week 48 (end of treatment)
4. Early virological response at week 12
5. Safety and compatibility of blood letting treatment in advance of a 48 week combination treatment with peginterferon alfa-2a/ribavirin

Completion date
30/06/2009

Eligibility

Key inclusion criteria
1. Aged 18 to 75 years
2. Serological evidence of chronic HCV genotype one infection with positive anti-HCV test
3. Evidence of a serum HCV-RNA concentration more than 10,000 IU/ml during screening measured with the COBAS AmpliPrep/COBAS TaqMan HCV Test (lower limit of detection 10 IU /ml)
4. No previous antiviral treatment
5. Ferritin level more than 200 µg/l
6. Liver puncture less than 24 months before the start of treatment
7. Compensated liver disease (Child - Pugh Grade A; evaluated in accordance with the clinical

classification of patients with cirrhosis)
8. In patients with cirrhosis or in transition to cirrhosis an ultrasound of the abdomen or another established method of excluding Hepatocellular Carcinoma (HCC) must be carried out within two months before the randomisation and the serum Alpha-Fetoprotein (AFP) value must be less than 100 ng/ml. In patients with a serum AFP value of more than 50 ng/ml, an established procedure must be used to exclude HCC
9. Negative urine or serum pregnancy test in women of childbearing age within 24 hours before taking the first dose of the drug
10. Whilst taking the study medication and during the 24 weeks after discontinuation, two recognised methods of contraception must be used, one of which must be a condom worn by the man to provide an effective barrier
11. The patient must be prepared and in a position for the regular checks within the framework of the trial to be carried out
12. A consent form must be signed after the trial has been explained

If one or more of these inclusion criteria do not apply, the patient may not be included in the study.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
65

Key exclusion criteria
1. Known hypersensitivity to peginterferon alfa-2a, alfa-interferons, ribavirin, or one of the other components of the product
2. Patients with any other HCV genotype except for genotype one
3. Women who are pregnant or breast feeding, women of child-bearing age who are not using contraceptives, and male partners of women who are pregnant or women of child-bearing age, who are not using contraceptives
4. Treatment with systemic antineoplastic or immune modulatory drug within the last six months before the start of the study and throughout the study. This includes treatment with histamine, mycophenolate mofetil, thymosin alpha, viramidin, levovirin and supraphysiological doses of steroids or radiation (with the exception of patients who have received limited treatment [seven days or less] of herpes lesions with aciclovir or valaciclovir more than one month before taking the first study medication)
5. Any other study medication within the last six weeks before the start of the first study measures (blood letting)

6. Positive evidence of Immunoglobulin M (IgM) antibodies to hepatitis A virus, hepatitis B surface antigens, IgM to hepatitis B virus, anti-Human Immunodeficiency Virus antibodies in the screening phase
7. Previous history or evidence of non-hepatitis C associated chronic liver disease (e.g. Haemochromatosis, autoimmune hepatitis, metabolic disorder of the liver, alcoholic liver disease or exposure to toxins)
8. Previous history or evidence of decompensated liver disease or a Child - Pugh Score more than six
9. Patients with increased risk of anaemia (such as thalassaemia, spherocytosis, a history of recurrent gastrointestinal bleeding etc.) or patients for whom anaemia would signify a particular medical risk
10. History of severe psychiatric illness, particularly severe depression. Severe psychiatric illness is defined as any history of at least three months continuous antidepressive or antipsychotic treatment or any evidence of suicidal tendency or referral to hospital as a result of psychiatric illness
11. Patients with known severe convulsions that cannot be stabilised with drugs
12. Auto-immune disease such as chronic inflammatory bowel disease, idiopathic thrombocytopenic purpura, lupus erythematosis, autoimmune anaemia, sclerodema, severe psoriasis, rheumatoid arthritis, etc.
13. Chronic pulmonary disease with functional limitation
14. Severe previous heart disease (e.g. heart failure in line with New York Heart Association (NYHA) class III or IV, myocardial infarction within the last six months, ventricular tachycardia requiring treatment, unstable angina, or other significant cardiovascular disease
15. History of organ transplant – excluding cornea transplant
16. Any severe disease, cancer or any other cause that in the estimation of the trial doctor makes the patient appear unsuitable for this study
17. Disorders of thyroid gland function that cannot be controlled with euthyroid medication
18. Evidence of severe retinopathy such as cytomegalovirus retinitis, macular degeneration or any clinically relevant ophthalmological diseases caused by diabetes mellitus or high blood pressure
19. Blood count: neutropenia less than 1,500 cells/µl and thrombocytopenia less than 75,000 cells/µl
20. Serum creatinine more than 1.5 mg/dl
21. Haemoglobin: less than 13 g/dl for men or less than 12 g/dl for women
21. Patients with intraventricular drug abuse or substitution treatment in the last 12 months
22. Patients with signs of hepatocellular carcinoma
23. Patients with a daily alcohol consumption of greater than 20 g
24. Any other previous illness which, in the judgement of the trial doctor, may jeopardise the completion of the treatment protocol
25. Patients who are uncooperative, do not understand the nature and structure of the study or do not sign the consent form

Date of first enrolment
01/04/2006

Date of final enrolment
30/06/2009

Locations

Countries of recruitment

Germany

Study participating centre
Heinrich Heine University Hospital
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Sponsor information

Organisation
Heinrich Heine University Hospital (Germany)

ROR
https://ror.org/024z2rq82

Funder(s)

Funder type
Industry

Funder Name
Roche Pharma AG (Switzerland)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	results presented at the AASLD meeting	30/09/2011	07/01/2021	No	No