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Safety and clinical effects of IDX320 in Hepatitis C infection

Submission date	Recruitment status	[_] Prospectively registered
17/03/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/03/2010	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
11/08/2011	Infections and Infestations	[_] 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

Protocol serial number
IDX-07A-001

Study information

Scientific Title
A Phase I/IIa Study Assessing Single and Multiple Doses of Hepatitis C Virus (HCV) Protease Inhibitor IDX320 in Healthy and Genotype 1 HCV-Infected Subjects

Study objectives

The safety profile and antiviral activity demonstrated in vitro and in vivo toxicology studies with IDX320 predicts acceptable safety in human subjects and safety and antiviral activity in Hepatitis C subjects.

Please note that as of 28/07/10 this record has been updated. All updates can be found in the relevant field with the above update date.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Netherlands: The local ethics committee (Stichting Beoordeling Ethiek Biomedisch Onderzoek) approved on the 22nd of January 2010

Added 28/07/10:
2. Poland: The local ethics committee (The Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym) approved on the 27 April 2010
3. Hungary: The Medical Research Council, Ethics Committee for Clinical Pharmacology approved on the 27 April 2010

Study design
Phase I/IIa randomised placebo controlled parallel group safety antiviral activity dosing study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Genotype 1 Chronic Hepatitis C

Interventions
Part A: single/multi dose escalation, food effect in healthy subjects; 8 subjects per cohort, randomized 6:2 (IDX320:placebo) to doses of 50 mg daily (QD) to 400 mg x 1 day and 400 mg x 3 days
Part B: single dose in HCV-infected subjects; 2 subjects total at 200 mg QD x 1 day
Part C: 3-day dose comparison in HCV-infected subjects; 30 subjects randomized 6:2 (IDX320: placebo) to doses from 50 mg QD x 3 days to 400 mg QD x 3 days
Part D: 3-day dosing in HCV-infected subjects; 6:2 (IDX320: placebo) at 200 mg twice a day (BID) x 3 days

Follow up for parts A and B is 6 days. Follow up for parts C and D is 28 days.
Please note for Parts C and D of the study (HCV-infected subjects), the Sponsor will reimburse peg-interferon and ribavirin costs for up to 48 weeks, following completion of the Day 4 assessments

Intervention Type
Drug

Phase

Phase I/II

Drug/device/biological/vaccine name(s)
IDX320

Primary outcome(s)
1. Safety and tolerability:
1.1. Adverse events, recorded at all study visits ie. Days 1-6 or 10
1.2. Physical examination performed at screening and Day 6 or 10 (depending on the Part of the study)
1.3. Vital signs, recorded at all study visits ie. Days 1-6 or 10
1.4. 12-lead ECG, performed at screening, Days -1, 1, 2, 4 and 6 for the single dose cohorts and at screening, Days -1, 1, 2, 3, 4, 7 and 10 for the multiple dose cohorts
1.5. Standard safety laboratory tests, performed at screening, Days -1, 1, 2, 4 and 6 for the single dose cohorts and at screening, Days -1, 1, 2, 3, 4, 7 and 10 for the multiple dose cohorts
2. Antiviral activity, measured at all study visits ie. Days 1-6 or 10 except Day 9:
2.1. Change in plasma HCV RNA
2.2. Emergence of resistance mutations

Key secondary outcome(s))
1. Pharmacokinetics:
1.1. Plasma and urine PK of IDX320
2. Food effect

Completion date
31/08/2010

Eligibility

Key inclusion criteria
1. 18-65 years of age, inclusive (or the legal age of consent per local regulations)
2. Body Mass Index (BMI) 18-35 kg/m2
3. Male subjects must have agreed to use a consistent form of an acceptable double-barrier method of birth control
4. Pulse ≥ 40 beats per minute (BPM), systolic blood pressure ≥ 95 mmHg and QTcF interval ≤ 450 ms at screening and Day -1
5. Subject has provided written informed consent to participate in the study
Part A Specific (must also meet the following)
6. Subject must be male.
Part C and D Specific (must also meet the following)
7. HCV treatment-naïve subject must have not received prior antiviral treatment for hepatitis C infection
Parts B, C and D Specific (must also meet the following)
8. Male or female subjects may be included. If female, subject must be of non-childbearing potential.
9. Documented clinical history compatible with chronic hepatitis C, including any one of the following:
9.1. anti-HCV antibody positive at least six months prior to screening or dosing OR
9.2. HCV ribonucleic acid (RNA) present in plasma by a sensitive and specific assay at least six months prior to screening or dosing OR
9.3. Histologic evidence of chronic hepatitis C infection (Note: Subjects with cirrhosis are

excluded)
10. Plasma HCV RNA ≥ 5 log10 IU/mL at screening
11. HCV genotype 1 by HCV genotyping performed at screening

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
Initial information at time of registration:
1. Co-infected with hepatitis B virus (HBV, HBsAg positive) and/or human immunodeficiency virus (HIV)
2. Donated blood or had significant blood loss 60 days prior to dosing
3. Use of alcohol and/or drugs that could interfere with adherence to study requirements as judged by the investigator
4. Positive screen result for drugs of abuse (except THC) or alcohol on Day 1
5. Concomitant use of any known major inhibitor or inducer of cytochrome P450 3A4 (CYP 3A4)
6. Use of other investigational drugs within 60 days of dosing, or plans to enrol in another clinical trial of an investigational agent while participating in the present study
7. Subject with intestinal malabsorption (e.g., structural defects, digestive failure or enzyme deficiencies with the exception of lactose intolerance)
8. Subject with known allergy to the study medication or any of its components
9. Clinically significant abnormal electrocardiogram (ECG) at screening or Day -1
10. Serum creatinine > Upper Limit of Normal (ULN)
11. Estimated glomerular filtration rate (GFR) < 60 mL/min/1.73 m2 as estimated by the Modification of Diet in Renal Disease (MDRD) formula
PART A Specific (following also excluded)
12. History of smoking more than 10 cigarettes (or equivalent amount of tobacco) per day within 3 months prior to admission to the Clinical Unit OR history of smoking within 24 hours prior to admission to the Clinical Unit
13. Any clinically significant medical condition that, in the opinion of the Principal Investigator, would jeopardize the safety of the subject or impact the validity of the study results
14. Concomitant use of prescription medications or systemic over-the-counter (OTC) medications. A washout period of at least 5 half-lives must be observed prior to study drug dosing, if the investigator feels that the medication can be safely discontinued for the duration of the study.
15. Abnormal laboratory values at screening or Day -1 that are considered to be clinically

significant by the Principal Investigator(s)
16. Positive screen for anti-HCV antibody
PART B Specific (following also excluded)
17. Subject received pegylated interferon and ribavirin within 6 months of screening
PART B, C and D Specific (following also excluded)
18. Subject is pregnant or breastfeeding. Women must have a negative serum beta-human chorionic gonadotropin (β-HCG) at screening and Day -1.
19. History or signs of decompensated liver disease: Child-Pugh class B or C, ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, or other clinical signs of portal hypertension or hepatic insufficiency
20. Prior clinical or histological evidence of cirrhosis (e.g. Metavir 4 or Ishak 6)
21. History of hepatocellular carcinoma (HCC) or findings suggestive of possible HCC
22. Active clinically significant diseases including:
22.1. Primary or secondary causes of liver disease (other than hepatitis C)
22.2. Malignant disease or suspicion or history of malignant disease within previous 5 years (except for adequately treated basal cell carcinoma)
22.3. Diabetes mellitus requiring treatment with medication
22.4. Any other condition that, in the opinion of the Principal Investigator, would jeopardize the safety of the subject or impact the validity of the study results
23. Previously received any other experimental direct-acting antiviral agents targeting the hepatitis C virus (e.g. HCV polymerase or protease inhibitors).
24. Requires frequent or prolonged use of systemic corticosteroids or other immunosuppressive drugs (e.g. for organ transplantation or autoimmune conditions). Topical or inhaled corticosteroids are permitted.
25. Abnormal values at screening or Day -1:
25.1. Alanine Aminotransferase ALT or Aspartate Aminotransferase AST > 5 x ULN
25.2. Any other laboratory abnormality that is considered to be clinically significant by the Principal Investigator(s)

Amended 28/07/10:
4. Positive screen result for drugs of abuse (except THC) or alcohol on Day 1, provided the positive test is not determined to be a false positive on confirmation testing or due to medically indicated prescription drugs

Date of first enrolment
08/02/2010

Date of final enrolment
31/08/2010

Locations

Countries of recruitment
Hungary

Netherlands

Poland

Study participating centre
Stationsweg 163
Zuidlaren
Netherlands
9471 GP

Sponsor information

Organisation
Idenix Pharmaceuticals (USA)

ROR
https://ror.org/02891sr49

Funder(s)

Funder type
Industry

Funder Name
Idenix Pharmaceuticals (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration