Telbivudine monotherapy for HIV-HBV coinfected patients: an open explorative study.

Published: 27-08-2008
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Monitoring of resitance development in HIV

Ethical review	Not approved
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Observational non invasive

Summary

ID

NL-OMON32543

Source
ToetsingOnline

Brief title
THH

Condition

- Viral infectious disorders

Synonym
hepatitis B; jaundice

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: HBV, HIV, telbivudine

Outcome measures

Primary outcome

Resistance development

Secondary outcome

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Study description

Background summary

Because HIV infection can accelerate progression of HBV-related liver disease, treatment of chronic hepatitis B is generally recommended for most HIV-infected persons with active HBV infection (e.g., elevated serum ALT level and HBV DNA >10,000 IU/mL). However, the best strategy for management of HBV infection has not been fully defined. Among patients with chronic HBV infection with no current indication for HIV treatment (e.g., CD4 cell count >350 cells/mm3), some experts recommend avoiding drugs active against HIV (e.g., emtricitabine, lamivudine, entecavir and tenofovir) and suggest using the use of adefovir, telbivudine and/or peginterferon. However, other experts recommend the institution of a fully suppressive antiretroviral regimen that includes the use of two agents active against HBV. This recommendation is based on the rationale that control of HIV infection may represent an important step in preventing HBV-related liver disease.
Therapy for HIV/HBV-coinfected patients for whom HIV treatment is indicated is less controversial; most experts recommend the use of an antiretroviral regimen that includes the use of two agents that are active against HBV (e.g., tenofovir plus emtricitabine or lamivudine).
Adefovir is a prodrug of tenofovir and although it has a high genetic barrier against resistance in HBV in acts slowly and after 24 weeks monotherapy in HBV monoinfected patients only 12-31 % reached an undetectable HBV load (1, 3). Moreover, given the activity of tenofovir against HIV adefovir harbors the possibility of inducing resistance (K65R mutation) in HIV. Therefore, it is not a very appealing drug for treatment of HBV/HIV coinfected patients. Pegylated interferon would be a possibility, especially in patients coinfected with HBV genotype A. However, given the serious adverse events and the fact that a considerable number of patients will develop lymfocytopenia, with a drop in the

already lowered CD4+ cells counts, many patients refuse therapy with peg-interferon.
Telbivudine (β-L-2'-deoxythymidine) is an orally bioavailable L-nucleoside with potent and specific anti-HBV activity. In preclinical toxicologic testing, telbivudine had no mutagenic or carcinogenic effects and no appreciable embryonic or fetal toxic effects * findings that are particularly relevant for men and women in their reproductive years. In initial clinical trials, treatment with telbivudine led to reductions in serum HBV DNA levels that were greater than those observed with lamivudine, and resistance to telbivudine developed less frequently than did resistance to lamivudine. Moreover, in a recent study it was shown that among patients with HBeAg-positive chronic hepatitis B, the rates of therapeutic and histologic response at 1 year were significantly higher in patients treated with telbivudine than in patients treated with lamivudine. In both the HBeAg-negative and the HBeAg-positive groups, telbivudine demonstrated greater HBV DNA suppression with less resistance than did lamivudine. At 24 wks 45% of HBeAg-positive patients had an undetectable viral load, while Hbe-Ag-negative patients had an even higher rate of undetectability (80%) (2, 3).
In another study in monoinfected HbeAg-positive patients Telbivudine demonstrated greater and more consistent HBV DNA suppression than adefovir after 24 weeks of treatment. After 52 weeks, HBV DNA suppression was greater in patients who had received continuous telbivudine or were switched to telbivudine after 24 weeks than in those who received continuous adefovir. Moreover, at week 24 39% of patients had an undetectable viral load compared to only 12 % of patients treated with adefovir. Telbivudine has no known activity against HIV and therefore we propose an explorative study in HIV/HBV coinfected patients not needing treatment of their HIV-infection with HAART.

Study objective

Monitoring of resitance development in HIV

Study design

Open explorative study

Study burden and risks

Extra blood samples in total 100 ml in 48 weeks

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

HIV infected no HAART and HBV infected needing treatment

Exclusion criteria

HAART indicated

Study design

Design

Study phase:	4
Study type:	Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-09-2008
Enrollment:	35
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Tyzeka®
Generic name:	Telbivudine
Registration:	Yes - NL intended use

Ethics review

Not approved

Date:	12-08-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2008-004409-33-NL
CCMO	NL24033.041.08