Nucleoside to Treat Multi-Drug Resistant Hepatitis B Infection

Published date: Aug. 12, 2016

Technology description

Background

Hepatitis B is a viral disease that affects the liver, causing a range in severity of symptoms, from mild, transitory illness to a serious, lifelong illness. Hepatitis B is spread when bodily fluids (such as blood or semen) from a person infected with the virus enters the body of someone who is not infected. This can happen through sexual contact or sharing needles or syringes, or other related equipment. Hepatitis B can also be passed from mother to child at birth. Hepatitis B can either be acute or chronic. Acute hepatitis B infection is a short-term illness that occurs within the first 6 months after someone is exposed to the hepatitis B virus. Acute infection can lead to chronic infection. Chronic hepatitis B infection is a long term illness that occurs when hepatitis B virus remains in a person's body. Chronic hepatitis B is a serious illness that can result in long term health problems, and even death.

Technology Summary

The present invention relates to the use of new carbocyclic nucleosides to treat or prevent infection with hepatitis B virus. This small molecule may be used for treatment of hepatitis B infection and secondary disease states such as cirrhosis and liver cancer, as well as a variety of other viral diseases. The compound exhibits potent in vitro activity against wild type virus and against triple mutant lamivudine-entecavir resistant strains, with a favorable Ec50 resistance profile. The prodrug was evaluated in chimeric mice infected with wild type and entecavir/lamivudine triple mutant viruses and reduced the serum HBV DNA level by 2.2 log copies in mice infected with the wild type clone, while mice infected with entecavir/lamivudine-resistant clone, a reduction of 1.2 log copies was observed.

Application area

Treatment of acute and chronic hepatitis B infection Prophylaxis for hepatitis B infection
Treatment of patents with multi-drug resistant hepatitis B infection
Treatment of hepatitis B and C co-infection

Advantages

Nucleoside reverse transcriptase inhibitor (NRTI) agent with potential effectiveness is drug-resistant HBV; in vivo evidence suggests efficacy in viral breakthrough of laminvudine-entecavir triple mutant

Product family includes a new nucleoside (FMCA) and a more potent nucleoside pohsphoramidate prodrug (FMCAP) as well as methods of synthesis
No significant mitochondrial toxicity seen in dosing (FMCA) up to 100uM (hepG2 cells)
Shown to reduce serum HBV DNA level by 2.2 log copies in mice infected with the wild type clone
Potent against lamivudine-entecavir triple mutants – reduced serum HBV DNA by 1.2 log copies in mice infected with entecavir/lamivudine-resistant clone
Prodrug form was unexpectedly found to be exceptionally active against drug resistant forms of hepatitis B virus

Institution

University of Georgia

Inventors

Jianing Wang
Chung Chu

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com