B-Fine: An open label, single arm study to mechanistically interrogate the therapeutic effect of GSK3228836 in patients with Chronic Hepatitis B via intrahepatic immunophenotyping

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Primary objective:To assess the effect of 12 weeks of GSK3228836 on serum hepatitis B virus surface antigen (HBsAg) levels in participants with CHBSecondaryEfficacy: To assess sustainability of serum HBsAg loss by GSK3228836 for up to 24 weeks off-…

Ethical review	Approved WMO
Status	Completed
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON52581

Source
ToetsingOnline

Brief title
studie:212602 B-Fine

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
Chronic Hepatitis B; Hepatitis B

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: CHB, Chronic Hepatitis B, Hepatitis B

Outcome measures

Primary outcome

The primary estimand is the percentage of participants with CHB receiving 300

mg GSK3228836 for 12 weeks (with at least one dose of IP) who achieve serum

HBsAg level
of PEG-interferon or other immunomodulator therapies, regardless of completing

IP, interruptions in IP or adherence to IP.

Secondary outcome

o Sustained HBsAg Response (HBsAg
GSK3228836 treatment

o Sustained HBsAg Response (HBsAg
GSK3228836 treatment

o Sustained Virologic Response (HBsAg
after the planned end of GSK3228836 treatment

All without the use of PEG-interferon or other immunomodulator therapies.

The effect of 12 weeks GSK3228836 on biomarkers and virus-specific antibody

responses:

• Achieving:

o HBsAg
o HBV DNA

o HBsAg and HBV DNA
• Categorical changes from baseline in HBsAg over time.

• ALT>3X ULN at over time

. HBe antibody (anti-HBeAg) levels over time

Variables:

• Actual values and change from baseline over time for HBsAg and HBV DNA

• HBs antibody (anti-HBsAg) and HBe antibody (anti-HBeAg) levels over time

• Area under the curve (AUC) for ALT on treatment (12 weeks), during follow up

(24 weeks), and on treatment + follow up (36 weeks).

Time to Event Variable

• Time to Maximum ALT (ALT must be greater than 3xULN) during 36 weeks of

treatment + follow up

Study description

Background summary

Functional cure of CHB occurs in a small percentage of patients on NA therapy alone. The high rate of relapse in these patients is hypothesised to be due to their inability to raise an effective immune response to the virus in the presence of high circulating levels of HBsAg. GSK3228836, was designed to inhibit the synthesis of HBsAg.Which may lead to (a higher percentage of patients with) functional cure of HBV.

B-Fine is an exploratory study of the therapeutic mechanism of GSK3228836 in participants with chronic hepatitis B (CHB) on stable nucleos(t)ide therapy. The study will investigate the virologic and immunologic correlates of HBsAg loss observed in participants when treated for 12 weeks with 300 mg GSK3228836. Repeat fine needle aspirates of the liver will be performed to enable analysis of liver-resident immune cells to investigate any

immunomodulatory properties of GSK3228836 and to study the biology of underlying treatment-associated liver flares. Longitudinal analyses of blood-borne inflammatory signatures and virological assessments of CHB infection will be performed in parallel.

Study objective

Primary objective:
To assess the effect of 12 weeks of GSK3228836 on serum hepatitis B virus surface antigen (HBsAg) levels in participants with CHB

Secondary
Efficacy:
To assess sustainability of serum HBsAg loss by GSK3228836 for up to 24 weeks off-treatment
To assess sustainability of serum HBsAg and HBV DNA loss by GSK3228836 for up to 24 weeks off treatment.
To assess the effect of 12 weeks GSK3228836 on biomarkers and virus-specific antibody responses

Study design

The study consists of a single treatment arm with 300 mg GSK3228836 for 12 weeks (loading schedule on Day 4 and Day 11). Participants will continue to receive their nucleoside therapy.

The total duration of the study, including screening, treatment and post-treatment follow-up, is not expected to exceed 45 weeks.
o 45-day screening window. Eligible participants who fall out of the 45-day window may be re-screened.
o Up to 1 week of pre-treatment assessments (including baseline FNA)
o 12 weeks treatment with GSK3228836
o 24 weeks post treatment follow-up (+ up to 10 days)

There are no plans for dose adjustments. Individual dose adjustments for safety are outlined in the monitoring/stopping criteria.

Intervention

Two 1 ml subcutaneous injections per visit, 14x

Study burden and risks

Known side effects of GSK3228836 based on past studies these side effects are considered very common (may affect more than 1 in 10 people):
• Reaction to injections including: pain, redness, swelling, and itching at or

near the site of injection
• Abnormal blood liver tests
• Increased body temperature, headaches, feeling sick, muscle pain

Other risks with GSK3228836, they are potential risks but not known as side effects for GSK3228836.
• Decreased platelet count/bleeding: in previous human studies, GSK3228836 did decrease platelet counts a little, but did not have any bleeding events.
• Drug induced vascular inflammation and complement activation, this effect has been seen in some animal studies with medicines like GSK3228836, but not in human studies with GSK3228836.
• Drug induced kidney injury, this effect has been seen in studies with medicines like GSK3228836, but not with GSK3228836.

Risks associated with stopping GSK3228836 treatment
• In hepatitis B patients, stopping nucleoside therapy has been known to cause abnormal blood liver tests. It is not known if stopping the study treatment (GSK3228836) will also cause increase in the results of blood liver tests
• Risk of the development of resistance to study drug
• With any drug against hepatitis B virus, there is a risk that the virus in your body will become resistant

Risks associated with study procedures/tests
• Blood drawls: giving blood might hurt ,give bruising, irritation or redness from the needle. Sometimes someone feels like faint.
• ECG: a skin rash or irritation may occur where electrodes were placed

Risks and complications of FNA may include:
• Pain and discomfort located at or near the puncture site and radiating upwards toward the right shoulder region, which may last for several hours after the procedure
• Bleeding at the biopsy site
• Possible internal bleeding for up to a few hours after the procedure (extremely rare - less than 1 in 10,000)
• Infections at the biopsy site or internal organs (extremely rare - less than 1 in 10,000
• Puncture of internal organs (gall bladder, lung, intestine or kidney) (less than 1 in 1,000),
• Significant bleeding requiring a blood transfusion or surgery to control the bleeding (extremely rare - less than 1 in 10,000),

Contacts

Public

GlaxoSmithKline

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Men and women >= 18 years of age
2. documented chronic HBV infection >=6 months prior to screening
AND currently receiving stable nucleotide analogue therapy (no changes to the nucleos(t)ide regimen from at least 6 months prior to screening and with no planned changes to the stable regimen over the duration of the study)
3. Plasma or serum HBsAg concentration >100 IU/mL.
4. Plasma or serum HBV DNA concentration must be adequately suppressed
5. HBeAg-negative
6. Alanine Transaminase (ALT) <=2 X ULN
7. A female participant: not pregnant or breastfeeding
8. of not childbearing potential or using a contraceptive method that is highly effective
9. male participant: refrain from donating sperm and use a sperm barrier during sexual intercourse

Exclusion criteria

1. Clinically significant abnormalities, aside from chronic HBV infection in medical history or physical examination
2. Co-infection with Current or past history of HCV or with HIV or HDV
3. History of or suspected liver cirrhosis and/or evidence of cirrhosis
4. Diagnosed or suspected hepatocellular carcinoma
5. History of malignancy within the past 5 years with the exception of specific cancers that are cured by surgical resection
6. History of vasculitis or presence of symptoms and signs of potential vasculitis
7. History of extrahepatic disorders possibly related to HBV immune conditions
8. History of alcohol or drug abuse/dependence
9. Currently taking, or took within 3 months of screening, any immunosuppressing drugs
10. Participants for whom immunosuppressive treatment is not advised, including therapeutic doses of steroids, will be excluded
11. Currently taking, or took within 12 months of screening, any interferon-containing therapy.
12. Participant requiring anti-coagulation

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	06-04-2021
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK3228836
Generic name:	GSK3228836

Ethics review

Approved WMO Date:	08-07-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-09-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-05-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	25-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2020-002000-39-NL
CCMO	NL74333.078.20

Study results

Date completed:	04-01-2022
Results posted:	15-04-2024

First publication
28-02-2024