A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Multi-Center Study Evaluating Antiviral Effects, Pharmacokinetics, Safety, and Tolerability of GS-5806 in Hospitalized Adults with Respiratory Syncytial Virus (RSV) Infection

Published: 13-10-2014
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON44628

Source
ToetsingOnline

Brief title
Gilead 1227

Condition

- Viral infectious disorders

Synonym
RSV infection

Research involving
Human

Sponsors and support

Primary sponsor: Gilead Sciences
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: GS-5806, Respiratory Syncytial Virus (RSV) Infection

Outcome measures

Primary outcome

The primary endpoint is the time-weighted average change in log10 viral load

from Baseline (Day 1) to Day 5 as measured by qRT-PCR.

Secondary outcome

The key secondary endpoints are:

- Time-weighted average change in the FLU-PRO score from Baseline to Day 5

- Duration of hospital stay following IMP administration

- Rate of unplanned medical encounters (clinic visits, emergency room visits,

urgent care visits, and rehospitalizations) related to a respiratory illness

after initial hospital discharge through Day 28

Additional exploratory endpoints are discussed in Section 3.1.

Pharmacokinetics:

- GS-5806 concentration in plasma at 2 hours +/- 30 minutes following IMP

administration

- GS-5806 concentration in plasma at Days 3 and 5

- The following plasma PK parameters will be calculated for GS-5806 (as

appropriate): Clast, Tlast, and AUClast.

Study description

Background summary

RSV infection is a cause of respiratory disease in the adult population. Respiratory syncytial virus (RSV), a member of the family Paramyxoviridae, is an enveloped virus with a negative single-strand ribonucleic acid (RNA) genome. Among adults, the 2 populations that are at higher risk for RSV infection are the immunocompromised and the elderly. Recently, RSV infection is becoming more recognized in the elderly population. RSV is responsible for 10.6%, 11.4%, 5.4% and 7.2% of hospitalizations for pneumonia, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), and asthma respectively. Currently there are no effective approved prophylactic or therapeutic treatment options for the adult population.

There is a significant unmet medical need for a safe, convenient, and effective treatment for RSV infection. The only approved antiviral therapy for RSV, ribavarin, is approved for use in pediatric populations, but is rarely used in clinical practice due to its limited efficacy and concerning safety profile. There is no approved antiviral therapy for RSV infection among adults, where the current standard of care is supportive.

Study objective

The primary objective of this study is to evaluate the effects of presatovir (GS-5806) on RSV viral load in RSV-positive adults hospitalized with acute respiratory infectious symptoms.

The secondary objectives of this study are to evaluate:
- The effect of presatovir on change in the FLU-PRO score from Baseline
- The effect of presatovir on the length of hospital stay
- The effect of presatovir on the rate of unplanned healthcare encounters (clinic visits, emergency room visits, urgent care visits, and rehospitalizations) related to a respiratory illness after discharge
- The pharmacokinetics (PK), safety, and tolerability of presatovir

Study design

Randomized, double-blind, placebo-controlled study evaluating the effect of GS-5806 on RSV viral load, PK, safety, and tolerability in hospitalized adults with RSV infection.

Intervention

GS-5806 50 mg tablets administered orally
- Dose Day 1 GS-5806: 200 mg (four 50mg tablets)

IMP must be administered after the subject has been fasting for at least 2 hours. The subject will remain in a fasting condition for approximately 1 hour after dosing.

Study burden and risks

In the study some assessments (such as blood samples, physical exam and urine collection) are related to this medical scientific research study and are additional to the treatment patients might have received if they would not participate in this study.

GS-5806 COMMON ADVERSE EVENTS
Presatovir has been given to almost 340 adults of whom 294 were healthy adult volunteers. Adults were treated with presatovir for as long as 7 days. No healthy adult treated with presatovir experienced a serious drug side effect or a side effect leading to stopping the study.
Adverse events reported by healthy volunteers who received presatovir are listed below:

Most Observed:
• Bloody nose 8%
• Diarrhea 4%

Less Observed:
• Rash, itchy 3%
• Headache 3%
• Lower value on breathing test 3%
• Constipation 3%

Least Observed:
• Common cold 2%
• Nausea 2%
• Dizziness 2%
• Rash, red 2%
• Stuffy nose 1%
• Sore throat 1%
• Lightheaded 1%
• Back pain 1%
• High liver function test 1%
• Stomach pain 1%

These adverse events were generally mild. Most cases of bloody nose and itchy rash were due to study related procedures such as nasal swabs and adhesive tape, and not the study drug.

There is always a l chance that people get an allergic reaction to a drug they have not taken earlier. Serious allergic reactions that can be life-threatening may occur. Some things that happen during any allergic reaction to any type of medication are:
• rash
• having a hard time breathing
• wheezing when you breathe
• sudden drop in blood pressure
• swelling around the mouth, throat, or eyes
• fast pulse
• sweating

Possible Side Effects of Study Procedures

Nasal Swabs: Inserting the swab into the patients nostril may cause discomfort, irritation, or a tickling sensation in the nostril. It can make patients cough or make their eyes water. Very rarely, the inside of the nostril may be irritated by the swab, which may cause slight bleeding. If this happens, the swab will be taken out right away.

ECGs: Sticky sensors called electrodes will be placed on the chest. After an ECG, there may be mild irritation, slight redness, and itches at the places on your skin where the sensors were placed. patients may have to have their chest shaved for this procedure.

Blood Samples: Drawing blood from a vein may cause local pain, bruising, occasional light-headedness, fainting, and very rarely, infection at the site of the blood draw

Urine Test: For females who could become pregnant, providing urine for a pregnancy test might make them feel embarrassed.

Questionnaires: Patients will fill out a questionnaire and the questions might make them feel uncomfortable or upset.
The study doctor or other study staff will fill out a health questionnaire and a health-care assessment form by asking them questions. Answering the questions might make them feel uncomfortable or upset.

UKNOWN/UNEXPECTED RISKS AND DISCOMFORTS
There may be other risks that do not happen often or that we don*t know about yet. This could include severe or life-threatening allergic reactions or

interactions with other drugs. Adverse events can sometimes be irreversible or fatal.

Contacts

Public
Gilead Sciences

East Blaine Street 199
Seattle WA98102
US
Scientific
Gilead Sciences

East Blaine Street 199
Seattle WA98102
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. >= 18 years of age at Screening
2. Willing to adhere to protocol specific requirements for contraception
3. Subject is a current inpatient
4. New onset of acute respiratory infectious symptoms,or acute worsening of chronic symptoms related to ongoing respiratory disease for <= 5 days prior to screening:
* Upper respiratory tract symptoms: Nasal congestion, runny nose, sore throat, or earache
* Lower respiratory tract symptoms: Cough, sputum production, wheezing, dyspnea, or chest

tightness
5. Documented to be RSV-positive as per protocol Section 6.1.1

Exclusion criteria

Related to concomitant or previous medication use:
1. Use of any investigational medicinal products in the 28 days prior to Visit 1, OR use of any investigational monocalonal antibody within 4 months or 5 half-lives of Visit 1 whichever is longer, OR use of any investigational RSV vaccine ever
2. Chronic use (> 28 days of use) of systemic immunosuppressive agents (see Section 4.3) during the 28 days prior to Screening, or anticipated use during the 28 days following Screening
3. Use of oral prednisone or other corticosteroid equivalent to:
- >20mg/day for > 14 days prior to screening is not permitted.
- >20mg/day for <= 14 days, including corticosteroids received during current hospitalization (ie, bolus doses), is permitted.
- <=20mg/day, regardless of duration, is permitted.
4. Subjects taking a moderate or strong cytochrome P450 (CYP) enzyme inducer including but not limited to rifampin, St John*s wort, carbamazepine, phenytoin, efavirenz, bosentan, etravirine, modafinil,and nafcillin within 2 weeks prior to the first dose of IMP;Related to medical condition:
5. Influenza positive as determined by local diagnostic test
6 Known MERS-CoV infection or known coinfection with other coronavirus;7. Subjects requiring > 50% supplemental oxygen (while subject is awake) at Screening
8. Subjects with a Clinical Frailty Score (CFS) > 7 at Baseline
8. Requirement for mechanical ventilation, not including noninvasive ventilation
9. Clinically significant bacteremia or fungemia that has not been adequately treated prior to Screening, as determined by the investigator.
10. Inadequate treatment of confirmed bacterial, fungal, or non- RSV pneumonia, as determined by the investigator
15. Excessive nausea/vomiting at admission, as determined by investigator, that precludes administration of an orally administered Investigational Medicinal Product (IMP)
16. Subjects with an unstable medical condition, as determined by the investigator, that precludes participation in the study;Related to allergies:
* Documented history of acute (anaphylaxis) or delayed (Stevens-Johnson syndrome or epidermal necrolysis) allergy to sulfa drugs

Study design

Design

Study phase: 2

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-03-2015
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GS-5806
Generic name:	presatovir

Ethics review

Approved WMO Date:	13-10-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-10-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	27-11-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-02-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2014-002137-58-NL
ClinicalTrials.gov	NCT02135614
CCMO	NL49680.056.14