A Phase 2b, Randomized, Controlled Trial Evaluating GS 5806 in Lung Transplant (LT) Recipients with Respiratory Syncytial Virus (RSV) Infection

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The primary objective of this study is as follows:* To evaluate the effect of presatovir (GS-5806) on nasal RSV viral load in RSV positive LT recipients with acute respiratory symptomsThe secondary objectives of this study are as follows: * To…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON43361

Source
ToetsingOnline

Brief title
GS-US-218-1797

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
respiratory infection, RSV infection

Research involving
Human

Sponsors and support

Primary sponsor: Gilead Sciences
Source(s) of monetary or material Support: Gilead Sciences;INC. 333 Lakeside Drive. Foster City;CA 94404

Intervention

Keyword: GS 5806, lung transplant, RSV infection

Outcome measures

Primary outcome

The co-primary efficacy endpoints are

* Time-weighted average change in log10 viral load from Day 1/Baseline through

Day 7 (DAVG7) as measured in nasal samples by RT-qPCR among subjects in the FAS

* Time-weighted average change in log10 viral load from Day 1/Baseline through

Day 7 (DAVG7) in a subset of FAS subjects whose duration of RSV symptoms prior

to the first dose of study medication is * median

Secondary outcome

Secondary endpoints are:

* Time-weighted average change in FLU-PRO score from Day 1/Baseline through Day

7

* Percent change from study baseline in FEV1% predicted value at Day 28/End of

Study

Study description

Background summary

Randomized, double-blind, placebo-controlled study evaluating the effect of presatovir on efficacy, PK, safety, and tolerability in LT recipients with RSV

infection.

Study objective

The primary objective of this study is as follows:
* To evaluate the effect of presatovir (GS-5806) on nasal RSV viral load in RSV positive LT recipients with acute respiratory symptoms

The secondary objectives of this study are as follows:
* To evaluate the effect of presatovir on clinical sequelae of RSV infection and on measures of lung function
* To evaluate the pharmacokinetics (PK), safety, and tolerability of presatovir

Study design

All subjects will be permitted to receive the standard-of-care therapy for RSV infection per their local medical practices, in addition to the investigational medicinal product (IMP).

Subjects will be randomized in a 2:1 ratio to receive presatovir administered as a 200-mg dose on Day 1/Baseline, followed by a 100 mg dose daily on Days 2 through 14, or placebo-to-match (PTM) once daily for a total of 14 days. All subjects will be stratified by 2 factors:
* Treatment of RSV infection (yes or no) with ribavirin (oral, intravenous, or aerosolized)
* Use of palivizumab or IVIG (yes or no)
At time of informed consent, subjects will be presented with the options to:
* Participate in optional DNA sampling for potential pharmacogenetic studies
* Participate in optional extended viral monitoring involving weekly nasal sampling for an additional 28 days after Day 28/End of Study (to Day 56). This sampling will be used to assess the duration of viral shedding and occurs only if the Day 21 nasal sample is PCR-positive or inconclusive for RSV.
* Participate in optional nasal sampling for gene expression analyses on Days 1/Baseline, 5, 7, and 21
* Participate in optional 48-week data registry involving collection of long-term clinical data to explore potential associations between RSV infection (and treatment) and the onset of lung transplant complications

Intervention

Subjects will be randomized in a 2:1 ratio to receive presatovir administered as a 200-mg dose on Day 1/Baseline, followed by a 100 mg dose daily on Days 2 through 14, or placebo-to-match (PTM) once daily for a total of 14 days.

Study burden and risks

Burden:
- Blood sampling: 6x
- Questions and questionnaires: every visit
- Nasale sample: every visit
- PK sample: 4x
- ECG: 2 or 3x
- saturation: 9x
- spirometry: 9x

There are risks involved with taking presatovir.

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. Most and less observed side effects reported by any presatovir healthy volunteer are listed below.

Most Observed
* Bloody nose 8%
* Diarrhea 4%

Less Observed
* Rash (itching) 3%
* Headache 3%
* Lower value on breathing test 3%
* Constipation 3%

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.

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

1) Males and females * 18 years of age who have received a LT (single or double) or heart/lung
transplant > 90 days prior to Screening
2) Confirmed to be RSV-positive by local polymerase chain reaction (PCR) testing (starting from when the upper or lower respiratory tract sample is obtained) * 7 days prior to IMP administration on Day 1/Baseline
3) New onset or acute worsening, if the symptom is chronic, of at least 1 of the following respiratory symptoms * 7 days prior to IMP administration on Day 1/Baseline: nasal congestion, earache, runny nose, cough, sore throat, shortness of breath, or wheezing
4) An informed consent document signed and dated by the subject
5) A negative local urine or serum pregnancy test for female subjects of childbearing potential
at Screening within 1 day prior to IMP administration. When available, existing local pregnancy test results obtained prior to Screening may be used, provided the testing was completed within 1 day prior to IMP administration.
6) Agreement from male and female subjects of childbearing potential who engage in heterosexual intercourse to use protocol specified method(s) of contraception as described in Appendix 6
7) Ability and willingness to complete necessary study procedures

Exclusion criteria

1) Use of any non-marketed (according to region) investigational agents within 30 days, OR use of any investigational monoclonal anti-RSV antibodies within 4 months or 5 half-lives of Screening, whichever is longer, OR use of any prior investigational RSV vaccines

2) Use of a strong or moderate cytochrome P450 enzyme (CYP) 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
3) Use of any of the following lympholytic treatment within the stated time frame: anti-thymocyte globulin (ATG), < 3 months; anti-lymphoblast globulin (ALG), < 3 months; muromonab-CD3 (OKT3), < 3 months; rituximab < 6 months; alemtuzumab < 9 months
Related to transplant history:
4) Recipient of any other organ transplant prior to Screening, with the exception of a LT (single or double) or heart/lung transplant
5) Recipient of a hematopoietic cell transplant at any time
6) Presence of BOS Stage 3 at Screening defined as a FEV1 of 50% or less of baseline
Related to medical condition at Screening:
7) Respiratory failure requiring invasive mechanical ventilation
8) Evidence of shock requiring vasopressors
9) Known viral coinfection (including but not limited to influenza, metapneumovirus, human rhinovirus, parainfluenza, cytomegalovirus, or coronavirus) in the upper or lower respiratory tract * 14 days prior to Screening unless discussed with the medical monitor and deemed acceptable
10) Active systemic infection or infectious pneumonia of any etiology (ie, bacterial, viral [other than RSV] or fungal), including aspiration pneumonia, that is considered clinically significant by the investigator unless discussed with the medical monitor and deemed acceptable
11) Pregnant or lactating females
12) Evidence of recent and rapidly deteriorating lung function, occurring before the onset of the
current viral respiratory infection, including but not limited to: acute lung allograft rejection, rapidly-progressive CLAD, and rCLAD (as determined by the investigator)
13) Any condition which, in the opinion of the investigator, would prevent full participation in this study or would interfere with the evaluation of the trial endpoints
Related to allergies:
14) Known hypersensitivity or allergy to the IMP, its metabolites, or formulation excipients (microcrystalline cellulose, mannitol, croscarmellose sodium, magnesium stearate, polyvinyl alcohol, titanium dioxide, polyethylene glycol and talc)
15) History of hypersensitivity, anaphylactic reaction, Stevens-Johnson Syndrome, or toxic epidermal necroylsis response to sulfa drugs
Related to laboratory values:
16) Clinically significant kidney dysfunction as defined by:
An estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m2 as calculated by the Modification of Diet in Renal Disease (MDRD) study 4 parameter equation obtained from screening laboratory measurements or via local laboratory measurements obtained * 7 days prior to Screening. The eGFR may be manually calculated or the reported eGFR value may be used, but any automatically calculated eGFR must be calculated using the MDRD equation.
17) Clinically significant liver function test abnormalities as defined by an ALT or AST > 5 times the ULN obtained in screening laboratory measurements or via local laboratory measurements obtained * 7 days prior to Screening

18) Clinically significant elevations in total bilirubin (TB), as determined by the investigator

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):	27-01-2017
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	presatovir
Generic name:	presatovir

Ethics review

Approved WMO

Date:	02-11-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	09-12-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-01-2017
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	EUCTR2015-002287-16-NL
CCMO	NL59391.078.16