A Phase 1b, randomized, partially double-blind, placebo-controlled study to assess the pharmacokinetics, safety, and tolerability of multiple doses of orally administered JNJ-53718678 in infants hospitalized with RSV infection

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Primary ObjectivesThe primary objectives are to evaluate in infants who are hospitalized with RSV infection:• the pharmacokinetics of JNJ-53718678 after multiple oral doses;• the safety and tolerability of JNJ-53718678 when administered for 7 days....

Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON43180

Source
ToetsingOnline

Brief title
JNJ-53718678 in Infants Hospitalized with RSV Infection

Condition

- Viral infectious disorders

Synonym
Respiratory syncytial virus infection, respiratory tract infection

Research involving

Human

Sponsors and support

Primary sponsor: Janssen Science Ireland UC
Source(s) of monetary or material Support: Janssen Science

Intervention

Keyword: Hospitalized, Infants, Infection, RSV

Outcome measures

Primary outcome

The primary endpoints are:

• the pharmacokinetic parameters of JNJ-53718678;

• the safety/tolerability data including, but not limited to, AEs, physical

examinations, vital

signs, ECGs, and clinical laboratory results.

Secondary outcome

The secondary endpoints are:

• RSV viral load as measured by qRT-PCR in nasal swabs will be used to

determine the following;

-AUC of RSV viral load over time;

-viral load over time, peak viral load, and time to peak viral load;

-proportion of subjects reaching undetectability of virus between first

administration of study drug and Day 28.

•RSV clinical course endpoints including:

-Length of hospital stay from admission to discharge;

-Need and duration of supplemental oxygen requirement (type and duration [h]);

-Need and duration of ICU stay;

-Need and duration of non-invasive ventilator support (eg, continuous positive airway pressure [CPAP]);

-Number of hours until saturation >92% on room air;

-Need and duration of endotracheal mechanical ventilation;

-Evolution of respiratory rate, SpO2, and body temperature;

-Evolution of RSV symptoms as assessed by the clinician COA;

-Amount of food intake, hydration, and feeding by IV.

Exploratory endpoints are:

• Evolution of RSV symptoms as assessed by the parent/caregiver COA;

• Relationship between various pharmacokinetic parameters and RSV clinical course and antiviral endpoints;

• Impact of viral genotype on antiviral response;

• Sequence analysis of the RSV F-gene before treatment (at baseline), during treatment, and post-treatment, as applicable;

• Presence of co-infections at Screening and detected retrospectively. The methodology that will be used to detect co-infections will be described in a separate laboratory manual;

• Time to clinical stability.

Study description

Background summary

RSV is considered the most important virus causing acute lower respiratory tract infection (LRTI) and is a major cause of hospital admissions and death in young children worldwide. Infants that are born prematurely or close to the RSV season and/or suffering from bronchopulmonary dysplasia or congenital heart disease are at the highest risk of developing severe RSV-related acute LRTI. In addition, RSV infection results in substantial illness and morbidity in the elderly and adults with underlying chronic illnesses, underlying disorders of cellular immunity, or suppressed immune systems.

Despite the large medical and economic burden, treatment options for RSV-associated bronchiolitis and pneumonia are limited: prophylactic treatment with passive immunization with the humanized monoclonal antibody palivizumab, treatment with ribavirin, and supportive treatment such as oxygenation and mechanical ventilation are available. There is an unmet medical need for prophylactic (pre- and post-exposure) as well as therapeutic treatment in both children and adults.

Study objective

Primary Objectives
The primary objectives are to evaluate in infants who are hospitalized with RSV infection:
• the pharmacokinetics of JNJ-53718678 after multiple oral doses;
• the safety and tolerability of JNJ-53718678 when administered for 7 days.

Secondary Objectives
The secondary objectives are to evaluate in infants who are hospitalized with RSV infection:
• the impact of JNJ-53718678 when administered for 7 days on the clinical course of RSV
infection, as assessed by the clinician;
• the antiviral activity of JNJ-53718678 when administered for 7 days.

Exploratory Objectives
The exploratory objectives are to assess in infants who are hospitalized with RSV infection:
• the relationship between the pharmacokinetics and the pharmacodynamics after repeated

oral dosing of JNJ-53718678 for 7 days;
• the evolution of viral resistance under JNJ-53718678 treatment;
• the impact of the viral genotype on the antiviral response;
• the impact of JNJ-53718678 when administered for 7 days on the clinical course of RSV
during and following hospitalization as assessed by the subject*s parent(s)/caregiver(s) in the
electronic clinical outcome assessments (COAs) through end of follow-up.

Study design

This is a Phase 1b, double-blind and placebo-controlled (except for the 1st cohort within each age group which is open-label), randomized, multicenter, multiple ascending dose study in infants who are hospitalized with RSV infection.

Intervention

Subjects will be dosed orally once daily (qd) or twice daily (bid), depending on the assigned dose regimen, during 7 days (Day 1-Day 7). Dosing should occur approximately at the same time(s) each day.

Each cohort in Part 1 will consist of 5 subjects (4 subjects receiving JNJ-53718678 and 1 subject receiving placebo), except for the first cohort of each age group which will contain only 4 subjects (4 subjects receiving JNJ-53718678). As such, each age group will include a minimum of 12 and a maximum of 20 subjects who will receive JNJ-53718678 treatment, and a minimum of 2 and a maximum of 4 subjects who will receive placebo, depending on the number of cohorts per age group.

Recruitment for Cohort f (Part 2 of the study) can start for a particular age group as soon as the last cohort of Part 1 for that respective age group has been completed through Day 7 and the safety/tolerability data and full pharmacokinetic data for the selected dose regimen has been reviewed and the DRC recommended the start of Cohort f for that respective age group. Dose and/or dosing regimen will be adapted or determined, as applicable, based on the review of the safety/tolerability and pharmacokinetic data integrating all data available at the time of the data review (completed and ongoing age groups/cohorts).

Study burden and risks

The subjects receive JNJ-53718678 during 7 days. Furthermore, nasal swabs and blood (max 5 times) will be taken from the subjects. The subjects will be in the hospital for two nights and visits will take place on day 7, 14 and 28

(will take 2 hours).

A recent study shows that children who are hospitalized, almost always are hospitalized at least 2 nights and often longer. So there is no additional burden on the hospitalization.
The total blood volume to be collected is considered to be in line with generally acceptable guidelines for the collection of blood samples for these age groups.11 For each pharmacokinetic sample 30 microliter of blood is required. The amount of blood for the safety samples will depend on local practice (eg, heel or finger prick versus venous sample), however sites are encouraged to limit the volume as much as possible.
The maximum amount of blood drawn from each subject for study-specific purposes will not exceed 3 mL/kg body weight over the duration of the study.
The other sampling (nasal swab) is kept as minimal as possible in order to keep the burden as low as possible.

No specific safety concerns were identified based on the currently available clinical data.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Each subject*s legally acceptable representative (ie, parent(s)/legal guardian/caregiver) must sign an ICF indicating that he or she understands the purpose of and procedures required for the study, are willing for their child to participate in the study, are willing for their child to remain in the hospital for the first 3 days of dosing (even if not clinically indicated), and are willing/able to adhere to the prohibitions and restrictions specified in the protocol (see Section 4.3) and study procedures.
2. Subject has presented at the hospital for suspected RSV infection within 72 hours prior to screening completion (ie, randomization).
3. Subject has been hospitalized for this suspected RSV infection.
4. Subject is a boy or a girl, who is >1 month to <=24 months of age on the day of randomization.
5. Subject has been diagnosed with RSV infection using a polymerase chain reaction (PCR)-based assay, preferably commercially available locally.
Note: in case there is no commercially available PCR-based assay at the site, the Sponsor should be consulted for agreement on the assay to be used.
6. Subject was born after a normal term pregnancy (>=37 weeks and 0 days).
7. With the exception of the RSV-related illness, subject is otherwise in good health without any significant medical illness on the basis of a medical evaluation that reveals the absence of any clinically relevant abnormality and includes a physical examination, skin examination, medical history, vital signs, ECG, and the results of blood biochemistry, blood coagulation, and hematology tests performed at Screening. If there are abnormalities, the subject may be included only if the Investigator judges the abnormalities or deviations from normal to be not clinically significant. This determination must be recorded in the subject*s source documents and initiated by the Investigator.
Note: Procedures that are standard of care and performed within 72 hours prior to screening completion (ie, randomization) may be used in determining study eligibility.

Exclusion criteria

1. Subject is upon current admission initially hospitalized in the ICU and/or in need of invasive endotracheal mechanical ventilation.
2. Subject has a history of any illness or a concurrent illness that, in the opinion of the Investigator, might confound the results of the study or pose an additional risk in administering study drug to the subject or that could prevent, limit or confound the protocol-specified assessments. This may include, but is not limited to, bacteremia, gross abnormalities, organ dysfunction, or severe comorbidity.
Note: The use of intravenous fluids is not exclusionary as long as the Investigator believes

the patient*s gastrointestinal tract still functions properly (i.e., is able to absorb drugs or nutrition).
3. Subjects who had major surgery within the 28 days prior to randomization or planned major surgery through the course of the study.
4. Subject has major congenital anomalies (eg, AV shunt) or known cytogenetic disorders (eg, Down*s syndrome).
Note: Open ductus arteriosus and open foramen ovale are not exclusionary as not considered major anomalies.
5. Subject has known or suspected immunodeficiency, such as known human immunodeficiency virus (HIV) infection.
6. Subject has known or suspected hepatitis B or C infection.
7. Subject has known allergies, hypersensitivity, or intolerance to JNJ-53718678 or its excipients.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	3
Type:	Anticipated

Ethics review

Approved WMO

Date:	16-06-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	26-09-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-01-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-01-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2015-002003-28-NL
ClinicalTrials.gov	NCT02593851
CCMO	NL57881.000.16

Study results

Results posted: 30-11-2018

Summary results
Trial never started

First publication
23-05-2018

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File