A Randomized, Double-blind, Placebo-controlled Study to Evaluate the Clinical Outcomes, Antiviral Activity, Safety, Tolerability, Pharmacokinetics, and Pharmacokinetics/Pharmacodynamics of JNJ-53718678 in Adult and Adolescent Hematopoietic Stem Cell Transplant Recipients with Respiratory Syncytial Virus Infection of the Upper Respiratory Tract

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To evaluate the clinical outcomes, antiviral activity, safety, tolerability, PK, and PK/PD of JNJ 53718678 in adult (ie, adult cohort) and adolescent (ie, adolescent cohort) HSCT recipients with an RSV upper respiratory tract infection (URT)I.The...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55100

Source
ToetsingOnline

Brief title
FREESIA RSV study

Condition

- Other condition
- Viral infectious disorders
- Respiratory tract infections

Synonym
RSV upper respiratory tract infections in HSCT patients / RSV upper airway infections in human stem cell transplant patients

Health condition

allogene / autologe hematopoietische stamceltransplantaties

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen Sciences Ireland UC (vertegenwoordig door Janssen-Cilag B.v. in Nederland)

Intervention

Keyword: Hematopoietic stem cell transplantation, Interventional clinical trial, Respiratory Syncytial Virus (RSV), Upper respiratory tract infection

Outcome measures

Primary outcome

To evaluate the effect of JNJ 53718678 on the development of RSV lower tract

respiratory infections (LRTIs) in adult hematopoietic stem cell transplant

(HSCT) recipients with RSV upper respiratory tract infection (URTI), as

measured by the proportion of participants who develop RSV LRTI (see definition

below) per the Endpoint Adjudication Committee (EAC)*s assessment through Visit

Day 28.

Secondary outcome

Proportion of Participants who Develop RSV-associated Lower Respiratory Tract

Complication (LRTC)

Number of Participants with Adverse Events (AEs)

Percentage of Participants with Abnormal Clinical Laboratory Findings

Percentage of Participants with Abnormal Electrocardiograms (ECGs) Findings

Percentage of Participants with Abnormal Vital Signs Findings

Proportion of Participants Progressing to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) and/or Death, in Participants who Develop RSV LRTI or RSV-associated LRTC per the EAC*s Assessment

Proportion of Participants Progressing to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive) and/or Death, (all-cause Mortality)

Proportion of Participants Progressing to Death (All-cause Mortality), in Participants who Develop RSV LRTI or RSV-associated LRTC per the EAC*s Assessment

Proportion of Participants Progressing to Death (All-cause Mortality)

Proportion of Participants Progressing to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive), in Participants who Develop RSV LRTI or RSV-associated LRTC per the EAC*s Assessment

Proportion of Participants Progressing to Respiratory Failure (of any Cause) Requiring Mechanical Ventilation (Invasive or Noninvasive)

Number of Supplemental Oxygen (O2) Free Days

Incidence of Supplemental Oxygen Requirement

Duration of Supplemental Oxygen

Change from Baseline in Respiratory Rate

Change from Baseline in Heart Rate

Change from Baseline in Peripheral Capillary Oxygen Saturation (SpO2)

Change from Baseline in Body Temperature

Proportion of Participants Hospitalized (of Participants who Were not Hospitalized at Baseline)

Proportion of Participants Re-hospitalized

Total Length of Hospital Stay

Total Time in the Intensive Care Unit (ICU)

Incidence of Grade 3 and Grade 4 Adverse Events (AEs)

Incidence of Respiratory AEs

Incidence of Thoracic-related AEs

Incidence of Antibiotic use in Participants who Develop and in Those who do not Develop RSV LRTI or RSV-Associated LRTC per the EAC*s Assessment

Time to Resolution of Symptoms as Assessed by Respiratory Infection Intensity and Impact Questionnaire (RiiQ) Symptom Scale

Change from Baseline in Severity of Symptoms Reported by Participants in the RiiQ Symptom Scale Through Day 28

Time to Resolution of Respiratory Illness as Assessed by Patient Global Impression of Severity (PGI-S) Scale

Change from Baseline in Patient Global Impression of Health (PGI-H) Scale Through Day 28

Change from Baseline in Patient Global Impression of Change (PGI-C) Scale Through Day 28

Area Under the Plasma Concentration-time Curve from Time Zero to 24 Hours Postdose (AUC [0-24]) of JNJ-53718678

Trough Plasma Concentration (Ctrough) of JNJ-53718678

Maximum Observed Plasma Concentration (Cmax) of JNJ-53718678

Association of Plasma Concentration-time Data of JNJ-53718678 and Antiviral Activity

Association of Plasma Concentration-time Data of JNJ-53718678 and Safety Parameters

Association of Plasma Concentration-time Data of JNJ-53718678 and Clinical Outcomes

RSV Viral Load and Change from Baseline Over Time

RSV Viral Load AUC from Immediately Prior to First Dose of Study Drug (Baseline)

Time to Undetectable RSV Viral Load

Proportion of Participants with Undetectable RSV Viral Load at Each Timepoint

Change from Baseline for the Health-related Quality of Life (HRQOL) as Assessed by 5-level EuroQol 5-Dimension (EQ-5D-5L) through Day 28

Change from Baseline for the HRQOL as Assessed by RiiQ Impact Scales Through Day 28

Change from Baseline in the RSV F Gene Sequence

Study description

Background summary

RSV is recognized as major respiratory pathogen in infants and young children and causes upper and lower respiratory illness among all age groups, often

going undiagnosed. Immunocompromised (IC) participants have a reduced ability to combat infection due to an impaired or weakened immune system. Within the IC population, HSCT recipients are generally regarded as having a particularly high risk for more severe disease caused by RSV, representing a substantial unmet need for antiviral treatment of RSV infections in this participant population. JNJ-53718678 is an investigational, potent small molecule respiratory syncytial virus (RSV) specific fusion inhibitor. The study will include a Screening Period (Day -2 to Day 1), a Treatment Period (Day 1 to Day 21), and a Follow-up Period (1 year). Assessments like chest X-ray, pulse/heart rate, respiratory rate, electrocardiogram (ECG), etc will be performed. Safety and efficacy will be assessed through the study. The total study duration for each participant will be approximately 49 days.

Study objective

To evaluate the clinical outcomes, antiviral activity, safety, tolerability, PK, and PK/PD of JNJ 53718678 in adult (ie, adult cohort) and adolescent (ie, adolescent cohort) HSCT recipients with an RSV upper respiratory tract infection (URT)I.

The primary objective of the study is to evaluate the effect of JNJ-53718678 on the development of RSV lower tract respiratory infections (LRTIs) in adult hematopoietic stem cell transplant (HSCT) recipients with RSV upper respiratory tract infection (URTI).

Study design

This is a Phase 2, randomized, double-blind, placebo-controlled, multicenter study to evaluate the clinical outcomes, antiviral activity, safety, tolerability, PK, and PK/PD of JNJ 53718678 in adult (ie, adult cohort) and adolescent (ie, adolescent cohort) HSCT recipients with an RSV URTI.

The study will include a Screening Period (Day -2 to Day 1), a Treatment Period (Day 1 to Day 21), and a Follow-up Period (1 year). The total study duration for each participant will be approximately 49 days, after which a long term follow up period takes place up to 1 year after start of study enrollment.

Intervention

Participants greater than or equal to (>=) 18 to less than or equal to (<=) 75 years of age will receive 250 milligram (mg) JNJ-53718678 twice daily (bid) for 21 days (without coadministration with moderate or strong CYP3A4 inhibitors), or 125 mg JNJ-53718678 bid for 21 days (coadministered with moderate or strong CYP3A4 inhibitors with the exception of posaconazole), or 125 mg once daily (qd) for 21 days (when coadministered with posaconazole), or matching placebo

for 21 days.

Study burden and risks

Side effects of standard of care, side effects of study assessments and side effects/unknown risks associated with the use of JNJ-53718678. throughout participation in this study. Study enrollments may result in additional hospital visits in comparison to the stand of care. It is possible that study-related visit may take longer than usual visits. Subjects are requested to complete a maximum of 11 study visits during a period of 49 days (outpatients), which is followed by a long term follow up period until 1 year after enrollment. A study visit may take approximately 1 - 2 hours, the screening visits takes approximately 4-5 hours. For patients that are hospitalized all study procedures are done during admission.

Several measures have been taken to safeguard the safety and health of study participants throughout the study.

The study will include the following evaluations of safety and tolerability:
- AEs
- clinical laboratory tests (central)
- ECG 12-lead
- vital signs: 1) vital signs assessments performed as part of the clinical course of RSV infection-related assessments (body temperature, heart rate, respiratory rate, and SpO2), 2)additional vital signs assessments: systolic blood pressure (SBP), diastolic blood pressure (DBP)
- physical examination of all body systems (at Screening) (including height and body weight measurements), direct physical examination, and skin examination

Clinically relevant findings resulting from the physical examination will be reported as AE. Safety and tolerability will be evaluated throughout the study from signing of the ICF until the last study related activity.

An Independent Data Monitoring Committee (IDMC) will be established to monitor and review data in an unblinded manner on a regular basis to ensure the continuing safety of the participants enrolled in this study. The committee will meet periodically to review safety data and will meet to review the results from the interim analysis. After the review, the IDMC will provide recommendations to the Sponsor Committee, who will be responsible for decision making, considering the IDMC recommendation, and who will communicate these decisions to the study team.

An interim analysis will be performed when approximately 50% of the planned participants in the adult cohort have completed the Day 28 assessments (or discontinued earlier). This interim analysis will include safety, testing for futility, early superiority, and a sample size re-estimation.

There are currently no direct-acting antiviral agent approved for prevention or treatment of RSV infections in HSCT recipients. Since RSV infections in at risk populations are associated with significant morbidity and mortality, there is a substantial unmet medical need for effective and safe treatments in HSCT recipients. This clinical trial will contribute to development of a potential new treatment to address this unmet medical need and may result in the registration of JNJ-53718678 as a treatment for RSV infections in an early stage.

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

- Male or female

- 18 to 75 years of age, inclusive

- Received an autologous or allogeneic hematopoietic stem cell transplant (HSCT) using any conditioning regimen

- Absolute lymphocyte count (ALC) less than (<) 1,000 cells/microliter (mL)

- Participant has laboratory confirmed RSV diagnosis within 48 hours of randomization

- New onset of at least 1 of the following respiratory symptoms within 4 days prior to the anticipated start of dosing: nasal congestion, rhinorrhea, cough or pharyngitis (sore throat), and/or worsening of one of these chronic (associated with previously existing diagnosis, example, chronic rhinorrhea, seasonal allergies, chronic lung disease) respiratory symptoms within 4 days prior to the anticipated start of dosing

- Peripheral capillary oxygen saturation (SpO2) greater than or equal to (>=) 92 percent (%) on room air

Exclusion criteria

- Admitted to the hospital primarily for a lower respiratory tract disease of any cause as determined by the investigator

- Requires supplemental oxygen at Screening or any time between Screening and randomization

- Documented to be positive for other respiratory viruses (limited to influenza, parainfluenza, human rhinovirus, adenovirus, human metapneumovirus, or coronavirus) within 7 days prior to or at the Screening visit, if determined by local SOC testing (additional testing is not required)

- Clinically significant bacteremia or fungemia within 7 days prior to or at Screening that has not been adequately treated, 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:	Completed
Start date (anticipated):	31-10-2019
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nap
Generic name:	nap

Ethics review

Approved WMO Date:	29-08-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-10-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	25-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-08-2021
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	EUCTR2019-001551-39-NL
ClinicalTrials.gov	NCT04221412
CCMO	NL71137.056.19

Study results

Date completed: 27-10-2021

Results posted: 24-01-2023

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

Internal documents
File