Study A: A placebo-controlled crossover study to assess safety of intranasal administration of palivizumab
Study B: Effect of intranasal administration of palivizumab on respiratory syncytial virus-associated infection - a double-blind randomized controlled trial

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Study A: Safety of intranasal administration of palivizumab in healthy adultsStudy B: Effect of local administration of palivizumab on prevention of RSV infection

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

Summary

ID

NL-OMON55390

Source
ToetsingOnline

Brief title
Narsyn: Nasal administration of palivizumab to prevent RSV infection

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
bronchiolitis, RSV respiratory tract infection

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: intranasal, prevention, respiratory syncytial virus

Outcome measures

Primary outcome

Study A: The main study outcome is self-reported symptoms according to the FDA scorecard and SAE*s. The phase IIb will be initiated based on the overall safety profile. The study will proceed to study B if no serious adverse events occur and other AE are considered non-related to treatment by the investigators and the DSMB.

Study B: The primary outcome is RSV infection with lab-confirmed RSV infection. RSV hospitalization is a key secondary outcome.

Secondary outcome

Study A: Observation of symptoms by a physician will take place for the 10 minutes following administration on the first day of intervention. We will test nasal swab samples for a respiratory panel to exclude the possibility of respiratory pathogen as the cause of symptoms when symptoms are present.

Study B: RSV hospitalization*, medically attended RSV infection without hospitalization, non-medically attended RSV infection, RTI hospitalization,

medically attended RTI without hospitalization, non-medically attended RTI, any hospitalization, otitis media, and wheeze in the first year of life. Incidence and total days of RSV-associated ICU stay, mechanical ventilation and supplemental oxygen suppletion, nasal swabs for co-infections by other respiratory pathogens if available, and safety data on local and systemic adverse events and severe adverse events.

*Key secondary endpoint

Study description

Background summary

Respiratory syncytial virus (RSV) is the second cause of death in the infant period after malaria worldwide. It is estimated that RSV was associated with 33,1 million cases of acute respiratory tract infection (ARTI) in 2015. Currently, there is no vaccine or treatment for RSV. Palivizumab, a humanized monoclonal antibody against the surface F protein of RSV, is the only approved preventive intervention, which is currently limited to high-risk infants due to prohibitive costs. To prevent one RSV hospitalization the current estimated cost for palivizumab is 100,000 euros. Not only are costs high, but prophylaxis is now administered via monthly intramuscular injections. The proposal to administer it via nose drops would make administration less burdensome for an infant and reduce costs by more than 90%. From 2008 - 2010, we performed a trial at the UMCU administering palivizumab to late preterms 32-35 weeks gestation age (WGA) and found an 80% reduction in hospitalization in the intervention group. We expect that local administration to the airways will be even more effective. Furthermore, in vivo we demonstrated that palivizumab can provide local mucosal protection when administered into the lungs to protect against RSV infection in a dose-dependent manner for up to a week after administration. We propose to administer palivizumab via the intranasal route (nose drops) to make it more affordable, acceptable and effective. The independent RSV patient advisory board (PAB) has specifically supported the importance of this study as they find it morally unacceptable that the current cost of RSV prevention is not only prohibitive, but also burdensome to young children with administration through 5 intramuscular injections.

Study objective

Study A: Safety of intranasal administration of palivizumab in healthy adults
Study B: Effect of local administration of palivizumab on prevention of RSV infection

Study design

Study A: Phase I RCT: Crossover safety study in healthy adult volunteers with 14-day washout period. After favorable DSMB evaluation, study B will start.
Study B: Phase IIb RCT: Double-blind placebo controlled proof-of-concept trial in target population.

Intervention

Study A: 1 nose drop in the right nostril once daily of 1 mg/mL palivizumab or placebo for 7 days; 14 day washout period, then crossover to other arm for 7 days.
Study B: 1 nose drop per nostril once daily of 1 mg/mL palivizumab or placebo for a duration of 2 - 5 months during the RSV season

Study burden and risks

Study A: This study is a phase I safety study. In the proposed population intramuscular palivizumab has been shown to be safe. There is no evidence that there is risk of toxicity upon intranasal administration for this monoclonal antibody that has a non-human target (RSV F protein) and has been used clinically for over 20 years.
Study B: This study is a therapeutic study. In the proposed study population palivizumab has been shown to reduce RSV-related hospitalization (82%), medically-attended RSV infection (80%) and total RSV infection (67%)[1]. Palivizumab is a registered drug for intramuscular administration that has an excellent safety profile and has been used clinically in children for more than 20 years. The burden is daily nose drops administered during the RSV season starting in October at the earliest for a duration of 5 months during the RSV season. The risks in this study are considered to be minimal. The possible benefit is prevention of RSV hospitalization, medically attended RSV infection and total RSV infection.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Study A: Healthy adults 18-60 years of age
Study B: 32-35 weeks gestational age with at least one brother or sister and less than 6 months old at the start of the RSV season

Exclusion criteria

Study A: Nasal obstruction, immunocompromised, respiratory symptoms or serious infection 4 weeks before study start, nasal surgery
Study B: known congenital heart disease, serious congenital disease, Down Syndrome

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2018
Enrollment:	408
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Synagis
Generic name:	palivizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-08-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-09-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-09-2018

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-04-2021

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 23402
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2018-002742-37-NL
CCMO	NL66735.041.18
OMON	NL-OMON23402
OMON	NL-OMON23479