Effect of palivizumab on respiratory syncytial virus-associated burden of disease - a randomized controlled trial

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

Summary

ID

NL-OMON47056

Source
ToetsingOnline

Brief title
Effect of palivizumab on recurrent wheeze

Condition

- Viral infectious disorders
- Thoracic disorders (excl lung and pleura)

Synonym
bronchiolitis, lower respiratory tract infection

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: AbbVie B.V.;follow-up 7 jaar;follow-up 6-8

jaar: MedImmune;aanvullend onderzoek antistoffen: financiering bij MedImmune aangevraagd

Intervention

Keyword: asthma, prevention, quality of life, respiratory syncytial virus

Outcome measures

Primary outcome

Number of wheezing days during the first year of life as noted in a log by

parents

Follow-up at the age of 6 year:

Determination or exclusion of asthma and allergy, transcriptome

Secondary outcome

Health-related quality of life determined with a validated questionnaire

(TAPQOL)

Long function testing and allergy testing, transcriptome analysis at age 6

years.

Whole genome methylation at age 7 years

Genome wide association study (GWAS) between the age of 6-8 years.

Additional research about specific antibodies against RSV

Study description

Background summary

Respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI) is the most frequent cause of bronchiolitis during infancy. Annually around 1500-2000 children are hospitalized with RSV-bronchiolitis. Prematurity is an important risk factor for RSV bronchiolitis. Long-term airway morbidity occurs in about half of hospitalized infants with RSV LRTI, which is referred to as

post-bronchiolitis wheeze (PBW). Prevention of severe RSV infection in preterm infants with gestational age <36 weeks is possible using monthly infection with palivizumab during the winter season. This effect of this humanized monoclonal antibody has been established in a large randomized controlled trial. In the Netherlands this drug is only used up to gestational age 32 weeks. Preterm children with gestational age 32-35 weeks are not prophylactically treated with palivizumab as decided by a national committee of pediatricians.

Study objective

It is not known whether recurrent wheeze in preterm children is caused by RSV infection (serial hypothesis) or that RSV infection is the first indication of chronic airway morbidity that would develop anyway (parallel hypothesis). This study aims to distinguish between these two hypotheses by investigating whether prevention of RSV (by palivizumab) results in decreased incidence of recurrent wheeze. We found a 61% reduction in wheezing days in the first year of life in children treated with palivizumab versus placebo. We will now expand planned tests at age 6. We will also perform lung function testing, allergic sensitization testing, transcriptome analysis and a nasopharyngeal swab. At the age of 7 years we will take a nasopharyngeal swab to provide further insight how a single virus may have long-term implications for epigenetic regulation of the respiratory epithelium and how integration of these different functions of the epithelium may be instrumental to understand asthma pathogenesis. Between the age of 6 and 8 years, a genome wide association study (GWAS) will be performed in order to investigate the contribution of genetic variation to RSV related short-term and long-term airway disease and the effectiveness of RSV-prophylaxis. If available after IgE measurement, we will test whether delayed first exposure to RSV infection by palivizumab results in different quality or quantity of IgG antibodies against the RSV F and G glycoproteins. Finally, we will test whether clinical diagnosis of asthma and decreased lung function have distinct serum protein biomarkers.

Study design

double-blind randomized controlled trial

Intervention

Monthly intramuscular injection with palivizumab (or placebo) during the winter months (October until February)

Study burden and risks

This study is a therapeutic study. Children who receive palivizumab will benefit the (established) beneficial prophylactic effect on the incidence of severe RSV infection. There are no known severe side effects. It is acceptable

that half of the study population receive placebo, because of the equal odds to receive palivizumab or placebo.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

gestational age 32-35 weeks

Exclusion criteria

known congenital heart disease
serious congenital disease
Down Syndrome

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-08-2008
Enrollment:	452
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	28-04-2008
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-07-2008
Application type:	First submission
Review commission:	METC NedMec
Approved WMO	

Date:	13-07-2009
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-06-2010
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-07-2010
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-09-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-01-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-07-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	05-12-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-03-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-07-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-03-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-04-2018
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-004105-10-NL
CCMO	NL18946.041.08
Other	NTR1023 / ISRCTN73641710