# Systemic Hydrocortisone To Prevent Bronchopulmonary Dysplasia in preterm infants.

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Is hydrocortisone safe and effective in reducing the incidence of the combined outcome death or BPD at 36 weeks PMA in chronically ventilated preterm infants, as compared to placebo.

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|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON26029

**Bron**
Nationaal Trial Register

**Verkorte titel**
SToP-BPD

**Aandoening**

Preterm infants
mechanical ventilation
BPD
Cortico steroids
hydrocortisone

### Ondersteuning

**Primaire sponsor:** Academisch Medisch Centrum Amsterdam
**Overige ondersteuning:** ZONMw

### Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Measure is survival free of BPD at 36 weeks postmenstrual age (PMA).

# Toelichting onderzoek

### Achtergrond van het onderzoek

Background:

Randomised controlled trials (RCTs) have shown that treatment of chronically ventilated preterm infants after the first week of life with dexamethasone reduces the incidence of bronchopulmonary dysplasia (BPD). However, there are concerns that its use may increase the risk of adverse neurodevelopmental outcome. Hydrocortisone has been suggested as an alternative therapy. So far no RCT has investigated its efficacy when administered after the first week of life to ventilated preterm infants.

Objective:

To establish the efficacy of hydrocortisone given after one week of life to reduce the incidence of the combined outcome death or BPD in chronically ventilated preterm infants.

Study design:

Randomised double blind placebo controlled multicenter study.

Study population:

Very low birth weight infants (GA < 30weeks and/or BW < 1250grams), ventilator dependent at a postnatal age of 7 – 14 days.

Intervention:

Administration of hydrocortisone or placebo during a 22 day tapering schedule.

Outcome parameters:

Primary outcome measure is survival free of BPD at 36 weeks postmenstrual age (PMA). Secondary outcomes are short term effects on the pulmonary condition, adverse effects during hospitalization, and long-term neurodevelopmental sequelae assessed at 2 years corrected gestational age (CGA).

Burden, benefit and risks associated with participation; group relatedness:

Burden: All infants participating in (either treatment arm of) the study are subjected to routine neonatal intensive care. The administration of the study intervention itself (hydrocortisone or placebo administration) does not pose an extra burden on the patients. This study does not require extra investigations or interventions.

Benefit and risks: Hydrocortisone may facilitate extubation and thereby reduce the total duration of mechanical ventilation. In addition, hydrocortisone may reduce the incidence of BPD. Both these beneficial effects may improve neurodevelopmental outcome. On the other hand, use of hydrocortisone may increase the risk for hyperglycemia, hypertension, systemic infection, gastrointestinal perforation and a delay in neurodevelopment. However, gastrointestinal perforation and delayed neurodevelopment have only been reported in studies administering corticosteroids in the first week of life and/or during combinations with other medication. In this study the risk of gastrointestinal perforation and delayed neurodevelopment may be reduced because hydrocortisone will be administered after the first week of life and will not be combined with other drugs that are known to increase the risk for these adverse effects. Infants assigned to the placebo group will not benefit from the aforementioned possible beneficial effects nor be subjected to the possible adverse effect of hydrocortisone.

Group relatedness: BPD is a complication occurring exclusively in preterm infants. Any intervention aiming to reduce the risk of this complication therefore needs to be studied in this specific population at risk.

## Doel van het onderzoek

Is hydrocortisone safe and effective in reducing the incidence of the combined outcome death or BPD at 36 weeks PMA in chronically ventilated preterm infants, as compared to placebo.

## Onderzoeksopzet

Inclusion 3 years;

Follow-up 2 years.

**Onderzoeksproduct en/of interventie**

Administration of hydrocortisone or placebo during a 22 day tapering schedule.

# Contactpersonen

## Publiek

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## Wetenschappelijk

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# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Preterm infants with:

1. A gestational age < 30 wks and/or birth weight < 1250 g;

2. Ventilator dependent at 7-14 days PNA;

3. A respiratory index (MAwP x FiO2) of ≥ 3.5 for more than 12 h/day for at least 48 hours, ensuring adequate oxygen saturation (85-95%) and pCO2 values in premature infants (5.0-7.5 kPa).

Of note: These target are used to ensure comparable assessment of MAwP and FiO2. After

inclusion of the patient in the study, physicians are free to use local targets for oxygenation and ventilation.

During the first 6 months of the trial it became clear that the Respiratory Index (RI) was set to high. Ventilated extremely preterm infants at high risk for BPD were not included in the trial because the RI was < 3.5. These infants were treated with corticosteroids outside the trial. Based on this observation the RI was first lowered to 3.0 in may 2012. As this only partly solved corticosteroids treatment outside the trial, the RI was further lowered to 2.5 starting december 2012. Following this last RI change, the majority of infants at high risk for BPD were eligible for the STOP-BPD study. All changes were approved by the Ethics Committee.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Chromosomal defects (e.g. trisomy 13, 18, 21);

2. Major congenital malformations that:

A. Compromise lung function (e.g. surfactant protein deficiencies, congenital diaphragmatic hernia);

B. Result in chronic ventilation (e.g. Pierre Robin sequence);

C. Increase the risk of death or adverse neurodevelopmental outcome (congenital cerebral malformations).

Of note: Intraventricular haemorrhages, periventricular leucomalacia and cerebral infarction are not considered congenital malformations and therefore are not exclusion criteria.

3. Use of dexamethasone or hydrocortisone for the sole purpose of improving lung function and respiratory status prior to inclusion.

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Dubbelblind |

| | |
|---|---|
| Controle: | Placebo |

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 01-09-2011 |
| Aantal proefpersonen: | 400 |
| Type: | Werkelijke startdatum |

### Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Nog niet bepaald

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 17-02-2011 |
| Soort: | Eerste indiening |

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register | ID |
|---|---|
| NTR-new | NL2640 |
| NTR-old | NTR2768 |
| Ander register | MEC AMC : 10/297 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

# Resultaten

**Samenvatting resultaten**
N/A