

# Therapy-efficacy of a new mode of Automatic Servo-Ventilation in patients with complicated breathing patterns during sleep

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<b>Registration date</b> 15/04/2010	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 13/07/2016	<b>Condition category</b> Nervous System Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Among the field of sleep-related breathing disorders (SRBD), there are different kinds of impaired breathing during sleep with different underlying causes. The most common kind of SRBD is obstructive sleep apnea (OSA), in which the upper airways collapse during sleep, preventing air from reaching the lungs, leading to an oxygen shortage and a build-up of carbon dioxide. The body reacts with a short awakening, restoring normal breathing until the next such event. The most effective treatment is continuous positive airway pressure (CPAP). A CPAP device produces positive pressure, applied to the patient's upper airways via a nasal or full-face mask which is worn during sleep. The increase in air pressure within the upper airways keeps them open and enables normal breathing.

Sleep apnea patients with heart failure often exhibit a different kind of SRBD, which may or may not exist in parallel to OSA. This condition is referred to as Cheyne-Stokes respiration (CSR). In CSR, too much breathing (hyperventilation) alternates with pauses in breathing (apneas). Depending on severity, this can occur for just a few minutes during the night or even during the whole night. This breathing disorder, even with co-existing OSA, can be treated with a further development based on CPAP, called auto-servoventilation (ASV). ASV devices apply changing pressure levels for the patient depending on current demand, not only providing a basic pressure to keep the airways open but also adapting pressure levels for inhalation and exhalation separately based on a breath-by-breath analysis of the patient's breathing volume. The aim of this study is to compare three different ASV treatment modes in sleep apnea patients with heart failure. One treatment mode uses the long-established BiPAP autoSV device (ASV2). The other two modes use the next device generation, BiPAP autoSV advanced (ASV3), in which a feature called Bi-Flex was introduced, which aims to provide smoother, more comfortable changes of pressure levels for inhalation and exhalation. ASV3 is used with either Bi-Flex on or off, forming the other two modes of treatment.

### Who can participate?

Heart failure patients with central sleep apnea, aged 40 to 80

What does the study involve?

Participants use the three ASV treatment modes in a randomly allocated order during consecutive nights in the study center's sleep lab. During these nights, sleep stages, breathing and other parameters are recorded. After these three treatment nights, the participants return home with the device and treatment mode they used during the last night. They then use the device at home every night and return to the study center after 1 month. At that time, we readout data from the device and ask patients about side effects, sleepiness and their quality of life using questionnaires. After 2 additional months of home use, the participants return to the sleep lab to undergo a final sleep study under treatment.

What are the possible benefits and risks of participating?

Possible benefits include more closely monitored treatment initiation and follow-up. Eligible patients for this study would normally (i.e. without participating in this study) be treated with the same or a similar device which is used in the study. For that reason, the possible risks of study participation essentially do not differ from routine clinical treatment.

Where is the study run from?

Wissenschaftliches Institut Bethanien eV (Germany)

When is the study starting and how long is it expected to run for?

January 2010 to January 2011

Who is funding the study?

Philips Respironics (France)

Who is the main contact?

Prof. Winfried Randerath

## Contact information

**Type(s)**

Scientific

**Contact name**

Prof Winfried Randerath

**Contact details**

Wissenschaftliches Institut Bethanien eV

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Solingen

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42699

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

## Secondary identifying numbers

EAME08ASV01

# Study information

## Scientific Title

Therapy-efficacy of a new mode of Automatic Servo-Ventilation in subjects with complicated breathing patterns during sleep: a multicentre randomised controlled trial

## Acronym

ASV3

## Study objectives

The new mode of Automatic Servo-Ventilation (Auto SV) with and without Bi-Flex® is as effective as the established mode of Auto SV in reducing respiratory events and arousals without adversely affecting sleep quality in subjects with heart failure and central sleep apnoea (CSA).

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

1. UK: South Birmingham Research Ethics Committee, 04/08/2009, ref: 09/H1207/119.  
Amendment 1 approved 29/12/2009
2. Germany: Ethik Commission der Univeritat Witten/Herdecke, 02/06/2009, ref: 110/2008.  
Amendment 1 approved 01/12/2009

## Study design

Multicentre randomised controlled double-blind cross-over pilot study

## Primary study design

Interventional

## Secondary study design

Randomised cross over trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## Health condition(s) or problem(s) studied

Central sleep apnoea/heart failure

## Interventions

Following an expiratory positive airway pressure (EPAP) determination study, subjects will be randomly assigned to one night of the new mode of Auto SV without Bi-Flex (ASV3 without Bi-Flex®), one night of the new mode with Bi-Flex® set at its maximum comfort level (ASV3 with Bi-Flex® set at 3) and one night of the established mode of Auto SV (ASV2) applied on consecutive nights in the sleep laboratory by the PSG technician under full PSG conditions. The first 2 hours of therapy (starting at lights out) will be spent at a sub-therapeutic pressure so that some breathing events are seen (EPAP = 4 cm H<sub>2</sub>O; IPAP<sub>min</sub>/IPAP<sub>max</sub> = EPAP). These studies will be performed within 14 days of the EPAP determination study. There will be a fixed follow-up period of 3 months.

## **Intervention Type**

Device

## **Primary outcome measure**

Variables investigated will include:

1. AHI (total, rapid eye movement [REM] and non-rapid eye movement [NREM]) - total, obstructive, central, and mixed (apnoea only) events (apnoea and hypopnoea)
2. Respiratory Disturbance Index (RDI): AHI plus respiratory effort related arousals (RERAs)
3. Cheyne-Stokes Respiration (CSR) Index - total
4. Arousal Index - total, respiratory, RERA and movement related
5. Sleep latency
6. Total sleep time
7. Wake, stages N1, N2, N3 and R sleep (% total sleep time [TST])
8. Wake, stages N1, N2, N3 and R sleep (in minutes)
9. REM latency
10. Number of REM periods
11. Mean REM interval
12. Mean pressure profile (EPAP, minimum inspiratory positive airway pressure [IPAP<sub>min</sub>], maximum inspiratory positive airway pressure [IPAP<sub>max</sub>])
13. Leak profile

All outcomes will be measured during each of the 3 therapy nights and on waking the following morning.

## **Secondary outcome measures**

1. Comfort will be improved on the new mode of Auto SV and further improved when Bi-Flex® is activated
  2. Subjects will rank the new mode of Auto SV higher than the established mode in terms of preference and the new mode of Auto SV highest when Bi-Flex® is activated
  3. The breathing event output from the new mode of Auto SV will result in an AHI (total) that is in diagnostic agreement with the apnoea-hypopnoea index obtained from a full clinical PSG
- All outcomes will be measured during each of the 3 therapy nights and on waking the following morning.

## **Overall study start date**

24/01/2010

## **Completion date**

20/06/2013

## **Reason abandoned (if study stopped)**

## Eligibility

### Key inclusion criteria

1. Apnoea Hypopnoea Index (AHI) greater than 15 (greater than 50% central events including central hypopnoeas) confirmed by full polysomnography (PSG) within last 14 days
2. Heart failure due to ischaemic, non-ischaemic or hypertensive cardiomyopathy (New York Heart Association [NYHA] Class II or III)
3. Aged greater than or equal to 40 - less than or equal to 80 years, either sex
4. Objectively impaired left ventricular ejection fraction greater than or equal to 40%, assessed by echocardiography
5. Stable clinical status and stable optimal medical therapy according to the guidelines of the European Society of Cardiology for at least 4 weeks ([www.escardio.org/knowledge/guidelines](http://www.escardio.org/knowledge/guidelines))
6. Able to provide consent
7. Able to follow the study protocol

### Participant type(s)

Patient

### Age group

Adult

### Sex

Both

### Target number of participants

36

### Key exclusion criteria

1. Positive airway pressure (PAP) therapy is otherwise medically contraindicated
2. Acute upper respiratory infection, encephalitis, sinusitis or middle ear infection or surgery of the upper airway, nose, sinus, or middle ear within the previous 90 days
3. Drug abuse (both acute and chronic) according to the Drug Abuse Screening Test (DAST) criteria
4. Alcohol abuse (both acute and chronic) according to the CAGE criteria
5. Intake of opioids or central relevant drugs, sedatives, or other drugs which impair sleep
6. Psychiatric or neurological diseases resulting in impairment of sleep, therapy or compliance
7. Thyroidal dysfunction
8. Any chronic pain syndrome
9. Acute pulmonary, and other internal diseases
10. Chronic pulmonary and other internal diseases resulting in impairment of sleep
11. Untreated, non-obstructive sleep apnoea (OSA)/CSA sleep disorders, including but not limited to; insomnia, periodic leg movements (PLM)/restless legs syndrome (RLS)
12. Previous exposure to positive airways pressure, bi-level or Auto SV therapy
13. Acute dermatitis or other skin lesions or trauma interfering with the application of a mask
14. Unwilling to participate in the study
15. Participation in another clinical study in the past 4 weeks

### Date of first enrolment

24/01/2010

**Date of final enrolment**

20/06/2013

## **Locations**

**Countries of recruitment**

England

Germany

United Kingdom

**Study participating centre**

**Wissenschaftliches Institut Bethanien eV**

Solingen

Germany

42699

**Study participating centre**

**Birmingham Heartland Hospital**

Sleep and Ventilation Unit

Department of Respiratory Medicine

Bordesley Green East

Birmingham

United Kingdom

B9 5SS

**Study participating centre**

**HELIOS Klinik Hagen-Ambrock**

Leitung Schlaflabor Pneumologie

Ambrocker Weg 60

Hagen

Germany

58091

## **Sponsor information**

**Organisation**

Philips Respironics (France)

**Sponsor details**

Immeuble HERMES  
20, rue Jacques Daguerre  
Rueil-Malmaison  
Paris  
France  
92565

**Sponsor type**

Industry

**Website**

<http://www.respironics.com>

**ROR**

<https://ror.org/05jz46060>

## **Funder(s)**

**Funder type**

Industry

**Funder Name**

Philips Respironics (France)

## **Results and Publications**

**Publication and dissemination plan**

To be confirmed at a later date

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not expected to be made available