



Clinical trial results: Improving GHB withdrawal with baclofen (The GHB Trial) Summary

EudraCT number	2013-005319-28
Trial protocol	GB
Global end of trial date	28 April 2017

Results information

Result version number	v1 (current)
This version publication date	13 May 2018
First version publication date	13 May 2018

Trial information

Trial identification

Sponsor protocol code	CNWL/AL/BACL/01
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Additional study identifiers

ISRCTN number	ISRCTN59911189
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Central and North West London NHS Foundation Trust
Sponsor organisation address	1st Floor, Bloomsbury Building, St Pancras Hospital, 4 St Pancras Way, London, United Kingdom, NW1 0PE
Public contact	Angela Williams , Central and North West London NHS Foundation Trust, baclofen.noclor@nhs.net
Scientific contact	Angela Williams , Central and North West London NHS Foundation Trust, baclofen.noclor@nhs.net

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2016
Global end of trial reached?	Yes
Global end of trial date	28 April 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Feasibility of a full scale RCT

Protection of trial subjects:

The study was conducted within ethical and regulatory framework. We acknowledged that the patient would have to spend some time with the researcher answering questions about how they feel, their medical and psychiatric history and having blood samples taken. To minimise any inconvenience and if face to face interviews were not possible or required, particularly at followup, participants were called. Whilst the risk from baclofen is minimal from our clinical experience, it was only given during benzodiazepine prescription and monitoring during detox. Whilst it can be safely prescribed to a wide range of people and is associated with few side-effects, we monitored those with some conditions as described in the SPC

Background therapy:

Benzodiazepine (diazepam)

Evidence for comparator:

GHB acts at GABAB receptors and therefore the GABAB agonist baclofen has been used on an unlicensed named patient basis as an adjunct to benzodiazepines to manage GHB/GBL withdrawal. Baclofen is currently only licensed in the UK for the management of muscle spasticity eg in multiple sclerosis. An uncontrolled case series in 19 GHB/GBL dependent patients, reported that baclofen (10mg tds) in addition to high dose diazepam during the initial 4–5 days of GHB/GBL detoxification, resulted in no transfers to ICU and several patients commented that baclofen was helpful. Additional clinical experience is that baclofen is helpful in reducing the complications from GHB/GBL withdrawal. Therefore it is suggested that baclofen (10mg tds) be used as an adjunct to benzodiazepines for GHB/GBL withdrawal. In addition our clinical experience is that starting baclofen two days before commencing medically assisted detoxification is helpful with anxiety and cravings as well as stabilising GHB use. Clinical experience is that baclofen is associated with few side-effects. Whilst a withdrawal state is recognised for baclofen, this is unlikely to occur with its use in acute GHB withdrawal due to the short duration (7–10 days) of baclofen use in this indication. We suggest that the risk of complications from baclofen withdrawal is considerably less than that of inadequately managed GHB/GBL withdrawal. Nevertheless, whilst use of baclofen holds promise, there are potential adverse effects on cardiovascular, neurological and respiratory systems so controlled data is urgently required to determine the efficacy and safety of baclofen in GHB/GBL withdrawal. Optimising outpatient treatment to reduce the risk of complications and hospital admission is important since many individuals decline admission. Despite this complexity and its impact on and cost to the individual and NHS, there is limited knowledge about how to best treat people in planned or unplanned GHB/GBL withdrawal.

Actual start date of recruitment	02 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 7
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Worldwide total number of subjects	7
EEA total number of subjects	7

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	7
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Individuals dependent on GHB requiring planned outpatient (Club Drug Clinic, CNWL) or unplanned inpatient detox (A&E, GSTT) were recruited between September 2016 to January 2017 (last participant recruited December 2016).

Pre-assignment

Screening details:

Participants were screened by telephone or in person regarding inclusion/exclusion criteria. Key: >18 years old who is either in active withdrawal or has underlying GHB/GBL dependence and wishes to undergo GHB/GBL detoxification or is thought to have underlying dependence and is at risk of acute withdrawal and able to take baclofen.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Blinding implementation details:

Study medication looked the same ie baclofen and placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Planned A

Arm description:

baclofen 10mg tds for 2 days then: benzodiazepine + baclofen 10mg tds

Arm type	Baclofen+baclofen
Investigational medicinal product name	baclofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

baclofen 10mg tds p.o.

Arm title	Planned B
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Arm description:

placebo tds for 2 days then: benzodiazepine + baclofen 10mg tds during detoxification

Arm type	placebo + active
Investigational medicinal product name	baclofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

baclofen 10mg tds p.o.

Arm title	Unplanned A
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Arm description:

benzodiazepine + baclofen 10mg tds during detox

Arm type	Active comparator
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Investigational medicinal product name	baclofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

baclofen 10mg tds p.o.

Number of subjects in period 1	Planned A	Planned B	Unplanned A
Started	2	4	1
Completed	0	2	1
Not completed	2	2	0
Physician decision	1	-	-
Adverse event, non-fatal	-	1	-
Lost to follow-up	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
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Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	7	7	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	7	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	5	5	

End points

End points reporting groups

Reporting group title	Planned A
Reporting group description: baclofen 10mg tds for 2 days then: benzodiazepine + baclofen 10mg tds	
Reporting group title	Planned B
Reporting group description: placebo tds for 2 days then: benzodiazepine + baclofen 10mg tds during detoxification	
Reporting group title	Unplanned A
Reporting group description: benzodiazepine + baclofen 10mg tds during detox	

Primary: Recruitment

End point title	Recruitment ^[1]
End point description: Recruitment number	
End point type	Primary
End point timeframe: Whole feasibility study	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This was a feasibility study with recruitment as a primary end point; the trial was terminated early and there is no statistical analysis.

End point values	Planned A	Planned B	Unplanned A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2 ^[2]	4 ^[3]	1 ^[4]	
Units: people	2	4	1	

Notes:

[2] - 2 people recruited and randomised to this arm

[3] - number recruited and randomised to this arm

[4] - number recruited and randomised to this arm

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All trial

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	2.1
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Reporting groups

Reporting group title	Planned A
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Reporting group description:

baclofen 10mg tds for 2 days then: benzodiazepine + baclofen 10mg tds

Reporting group title	Planned B
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Reporting group description:

placebo tds for 2 days then: benzodiazepine + baclofen 10mg tds during detoxification

Reporting group title	Unplanned A
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Reporting group description:

benzodiazepine + baclofen 10mg tds during detox

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events were reported in the total of 7 participants recruited

Serious adverse events	Planned A	Planned B	Unplanned A
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
Drug withdrawal syndrome			
subjects affected / exposed	0 / 2 (0.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Planned A	Planned B	Unplanned A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 4 (0.00%)	0 / 1 (0.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 September 2015	<p>inclusion criteria: Drug services will assess the whole needs of the individual and work in partnership with other services to ensure that drug and alcohol use is seen in the context of agreed aftercare plan and the complexity of participant's lives.</p> <p>Revised sample size: Due to issues regarding IMP and funding envelope available, our sample size was reduced for unplanned detoxification group only (Medical Toxicology, St. Thomas's Hospital, London site) from 40 patients to 28 patients (14 patients in each arm). The planned group recruited from CNWL Club Drug Clinic site remains at 60.</p> <p>Weekend assessment: For planned detoxification group at CNWL Club Drug Clinic, we initially proposed that two of the assessments, CIWA-Ar and Sedation Assessment Tool, will only be completed during weekday clinic visits and not during weekends. However, we will give two printed copies of these assessments to our participants on Friday (Day 5 of detox) so they can complete them each day at home during the weekend and bring them back on Monday (Day 8 of Detoxification). This will enable us to collect robust data for the entire detox period including weekend.</p> <p>Focus groups to individual interviews for participants.</p> <p>Weekly follow-up contact via telephone.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 January 2017	Recruitment was halted to review the overall risk- benefit relationship of continuing the trial. The study did not re-start.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This was a feasibility study that terminated early. The primary objective was to look at recruitment to inform a main RCT. The study was not powered to compare treatment arms . No statistical analysis was conducted.

Notes: