ISRCTN33042138 https://doi.org/10.1186/ISRCTN33042138

Intravenous immunoglobulin in the treatment of primary trigeminal neuralgia refractory to carbamazepine

Submission date	Recruitment status	[X] Prospectively registered
14/10/2002	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
14/10/2002	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
17/08/2018	Nervous System Diseases	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Andreas Goebel

Contact details
The Walton Centre NHS Trust
Lower Lane
Fazakerley
Liverpool
United Kingdom
L9 7LJ

Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title

Low-dose intravenous immunoglobulin or 0.9% saline in the treatment of primary trigeminal neuralgia refractory to carbamazepine: a randomised double blind parallel placebo-controlled multicentre trial in an outpatient setting

Study objectives
Added 15/09/2008:
We hypothesise that intravenous immunoglobulin (IVIG) is more effective to relieve pain from trigeminal neuralgia (TN) than 0.9% saline placebo.

Please note that as of 15/09/2008 this record has been extensively updated. These changes are due to the withdrawal of the initially proposed source of funding after registration in 2002, but prior to the projected study start date in 2003. Therefore, once a new source of funding was found the investigators took the opportunity to further improve on the study design. All updates and additions to this record can be found in the relevant sections, under the above update date. Please note that the trial is now taking place in the United Kingdom instead of Germany (where the initial sponsors were based), and the target number of participants has now changed to 32 participants due to a new sample size calculation being performed. The previous number of participants was 64.

Please also note that due to this change, the trial start and end dates were pushed back. The initial anticipated start and end dates of this trial were as follows:
Initial anticipated start date: 14/10/2003
Initial anticipated end date: 14/10/2005

Ethics approval required
Old ethics approval format

Ethics approval(s)
Added 15/09/2008:
The Joint UCL/UCLH Committees on the Ethics of Human Research (Committee A), London granted approval on the 13th March 2008

Study design
Placebo controlled, parallel, add-on model

Primary study design
Interventional

Study type(s)
Not Specified

Health condition(s) or problem(s) studied
Trigeminal neuralgia

Interventions
Added 15/09/2008:
Treatment with three applications of 0.5 g/kg IVIG or normal saline

Initially proposed interventions:
Treatment with three applications of 10 g IVIG or normal saline

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Intravenous immunoglobulin

Primary outcome(s)
Initially proposed outcome:
Primary outcome variable defined as the length of time during which patients remain in the study. Study groups are compared using Kaplan-Maier survival analysis. Patients record their response to treatment ("severe, moderate, slight, no pain"). The study coordinator monitors pain diaries. Severe or moderate pain of three days duration will result in termination of the study for that patient.

Added 15/09/2008:
The primary outcome measure for a patient is whether he/she drops out of the trial before day 14 (day 1 is the 1st day of infusion). A patient dropping out before day 14 is labelled a failure. Patients are removed from the trial as per protocol: "If from study day 6 at any time for three consecutive days the average pain intensity is noted either as 'severe' or as 'moderate'. If noted as 'moderate' the patients overall impression of change is less than 'much improved' on the 'impression of change' scale."

Key secondary outcome(s))
Added 15/09/2008:
1. The report by a patient of a significant reduction in the number of those attacks ('paroxysms') with a pain intensity of greater than 4 NRS. Significant reduction is defined as a greater than 75% reduction of spontaneous attacks and a greater than 50% reduction of evoked attacks. This is measured over 24 hours at:1.1. Day 8, and 1.2. In addition on day 13 (intention to treat analysis for day 13)
2. The global impression of change as noted for the period starting from day 9 to day 13 inclusive (intention to treat analysis)

Completion date
01/06/2010

Eligibility

Key inclusion criteria
Patients suffering from primary trigeminal neuralgia refractory to carbamazepine therapy

Added 15/09/2008:
Patients are suitable for consideration for screening and enrolment if they have received a diagnosis of primary trigeminal neuralgia (TN) according to International Headache Society criteria including both 'classical TN' and with features of 'atypical TN', provided they initially presented with 'classical TN'. For clarity, these criteria are listed here:
A. Paroxysmal attacks of pain lasting from a fraction of a second to 2 minutes, affecting one or more division of the trigeminal nerve and fulfilling criteria B and C

B. Pain has at least one of the following characteristics:
1. Intense, sharp, superficial or stabbing
2. Precipitated from trigger areas or by trigger factors
C. Attacks are stereotyped in the individual patient
D. There is no clinically evident neurological deficit
E. Not attributed to another disorder

Patients are suitable if they report a dull, burning pain after the shooting paroxysms that then also disappears (atypical form). In addition, there may be a constant element to the pain, but only if in the judgement of the consultant pain specialists responsible for enrolling the patient this patient has had on initial presentation a credible diagnosis of classical trigeminal neuralgia (without a constant element). In addition, patients are also suitable if they have a neurological deficit that is considered by the respective consultant grade site investigator to have emerged following an interventional procedure aimed at relieving pain from trigeminal neuralgia. Patients who have had previous successful surgical treatments but who have suffered a recurrence of classical or atypical trigeminal neuralgia or have developed a constant element to their pain are suitable. Patients on a stable dose of antiepileptic drugs are suitable. Treatment with antiepileptic drugs prior to enrolment will be noted, but prior treatment with antiepileptic drugs other than carbamazepine is not a prerequisite for consideration for screening and enrolment.

Patients fulfilling the above listed suitability criteria may be screened if they:
1. Are willing to participate in the study as evidenced by giving written informed consent and willingness to return to the study site at the intervals specified in the protocol
2. Are male or female above 18 years of age
3. Are females and there is evidence that they are not pregnant or lactating or that they are post-menopausal. A urine pregnancy test will be performed on the day of the first infusion if no other credible evidence such as of either sterilisation or post-menopausal status is given. Confirmation of the use of adequate birth control will be required in pre menopausal women, which give no evidence for an inability to become pregnant.
4. Have no physical condition, which, in the opinion of the investigator, is unstable or would otherwise prevent the patient from completing the study.
5. Have sufficient cognitive function and English language skills to complete questionnaires, keep a daily diary, use an electronic diary, and communicate verbally with the nursing staff. English language skills are required because not all the questionnaires have been translated or validated in other languages.
6. Are receiving a stable dose of an antiepileptic drug, with adequate pain control, but experience a poor side-effect profile, as judged by both the patient (documented at the first appointment by ticking 'non-acceptable' to a question: 'do you consider side effects from your medication taken for pain acceptable non acceptable') and the consultant-grade site investigator.

Patients will:
1. Have an average 24-hour pain severity of greater than 4 on a numeric scale of 0 - 10 during the seven day screening period, and
2. At least have moderate pain on each day of that period on a scale none-mild-moderate-severe, and
3. Have at least an average of 35 pain paroxysms with an intensity of Numerical Rating Scale (NRS) greater than 4 during the seven day screening period

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Added 15/09/2008:
Following patients with facial pain are not suitable for inclusion:
1. Trigeminal neuropathic pain defined by a main component of continuous pain (even if shooting /sharp pains superimposed)
2. Symptomatic TN (multiple sclerosis [MS], tumour)
3. Concomitant non-neuropathic pain which is moderate/severe (e.g., temporomandibular disorder [TMD])
4. Sharp, shooting pain and autonomic symptoms (= trigemino-autonomic cephalalgias)
5. Patients with frequent spontaneous remissions as judged by the treating consultant
6. Typical/atypical TN waiting for surgery which is imminent (within less than 4 months)

Date of first enrolment
01/08/2008

Date of final enrolment
01/06/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Walton Centre NHS Trust
Liverpool
United Kingdom
L9 7LJ

Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Industry

Funder Name
Added 15/09/2008:

Funder Name
Talecris Biotherapeutics (USA) - supplied a competitive research grant

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	study protocol	30/01/2003		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes