

# Double-blind randomised placebo-controlled cross-over study to investigate the safety and effectiveness of intrathecal glycine on pain and dystonia in Complex Regional Pain Syndrome type 1

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<b>Registration date</b> 09/01/2006	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 18/08/2009	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Protocol serial number**  
NTR499; P05.108

# Study information

## Scientific Title

## Acronym

The ITG study (ITG is an abbreviation for intrathecal glycine)

## Study objectives

A large proportion of chronic patients with complex regional pain syndrome type 1 suffer from both neuropathic pain and dystonia. Findings from neurophysiological and intrathecal baclofen studies highlight an impaired inhibitory neurotransmission. Since glycinergic neurotransmission plays an important inhibitory role in afferent and motor processing, glycine administration may offer new options for the treatment of both pain and movement disorders in patients with CRPS I.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Received from local medical ethics committee

## Study design

Randomised double blind placebo controlled crossover group trial

## Primary study design

Interventional

## Study type(s)

Treatment

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

Complex regional pain syndrome type 1 (CRPS I)

## Interventions

For future intrathecal baclofen treatment, in all patients a programmable pump for continuous intrathecal administration (SynchroMed® pump, Medtronic, Minneapolis MN, USA, 40 ml reservoir) and a lumbar reservoir for cerebrospinal fluid sampling will be implanted.

Each subject receives two treatments:

1. 2.1% glycine solution during 4 weeks

2. Sodium chloride 0.9% during 4 weeks (placebo)

Study treatment is started at a dosage of 8/21 ml/24 hours (during treatment with glycine 2.1% this corresponds to 8 mg/24 hours) and will be weekly increased with 8/21 ml/24 hours.

There is a tapering and wash-out period after each treatment: tapering in 1 week (3 equal dose decreases with an interval of 48 hours e.g. Monday 22, Wednesday 12 and Friday 0 mg/24 hours) and wash-out in 1 week.

Treatment is started on Mondays.

## Intervention Type

Other

## **Phase**

Not Specified

## **Primary outcome(s)**

Primary outcome is the safety of ITG.

Safety evaluations include history taking, physical examination and neurological examination, blood and cerebrospinal fluid assessments and 12-lead electrocardiography (ECG).

## **Key secondary outcome(s)**

Secondary outcome is the efficacy of ITG compared to placebo.

Patients are assessed: 2 weeks before pump implantation, during both treatments at days 1, 8, 15, 22 and 29.

At days of dose adjustment, assessments are performed first.

These assessments include:

1. Movement disorders assessments:

1.1. Visual analogue (VAS) dystonia scale: self-assessed every Monday at 9:00, 14:00 and 20:00 from 2 weeks before pump-implantation to the end of the study. Symptom severity is rated from 0 (absent) to 10 (most severe).

1.2. Standardised measures are:

1.2.1. The Fahn-Marsden dystonia rating scale

1.2.2. Barry-Albright Dystonia scale

1.2.3. Unified myoclonus rating scale (sections 2, 3, 4, 5, 7 and 8)

1.2.4. Tremor research group rating scale

Assessed 2 weeks before pump implantation and during both treatments at days 1, 8, 15, 22 and 29.

1.3. Change of dystonia is rated on a global impression scale. The blinded investigator assesses the change from baseline on a global impression scale at the end of both treatments.

2. Sensory assessments:

2.1. VAS pain scale: self-assessment (as VAS dystonia scale)

2.2. McGill pain questionnaire: assessed every Monday from 2 weeks before pump-implantation to the end of the study

2.3. Thermal sensory analyzer: to assess pain and temperature perception thresholds (Medoc Ltd, Israel, model TSA-II, using the method of limits) and is done during both treatments at days 1 and 29. A thermode is placed on the volar side of the wrists (if involved) and the dorsal side of the feet (if involved).

3. Activity level:

3.1. Radboud Skills Questionnaire: in case of involvement of upper extremities

3.2. Walking Ability Questionnaire: in case of involvement of lower extremities

## **Completion date**

21/11/2007

## **Eligibility**

### **Key inclusion criteria**

1. Patients must fulfil the diagnostic criteria of the consensus report of CRPS I:

1.1. Continuing pain, allodynia or hyperalgesia, in which the pain is disproportionate to any inciting event

1.2. Evidence at some time of edema, changes in skin blood flow or abnormal sudomotor activity

in the region of the pain

- 1.3. No condition that would otherwise account for the degree of pain and dysfunction
2. Patients must suffer from clinically significant tonic or intermittent dystonia in one or more extremities
3. Patients must have symptoms for at least 1 year

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

All

**Key exclusion criteria**

1. Patients are excluded if they can obtain satisfactory relief of symptoms with conventional treatments
2. Patients with a history of alcohol or drugs abuse within the past year
3. Patients with clinically significant psychiatric illness
4. Pregnant, nursing women and females of childbearing potential not using effective contraception
5. Patients who are unlikely to comply with study requirements or have a history of poor compliance to medical regimens or study requirements
6. Patients with an insufficient command and understanding of the Dutch language
7. Patients involved in legal proceedings (claiming compensation for their CRPS I)

**Date of first enrolment**

21/11/2005

**Date of final enrolment**

21/11/2007

**Locations**

**Countries of recruitment**

Netherlands

**Study participating centre**

**Leiden University Medical Center**

Leiden

Netherlands

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# Sponsor information

## Organisation

Leiden University Medical Centre (Netherlands)

## ROR

<https://ror.org/027bh9e22>

# Funder(s)

## Funder type

Government

## Funder Name

Ministry of Economic Affairs (Netherlands)

## Alternative Name(s)

Ministry of Economic Affairs, Netherlands Ministry of Economic Affairs, EZ

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

Netherlands

# 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?
<a href="#">Results article</a>	results	01/11/2009		Yes	No