



Clinical trial results:

Local treatment of craniomandibular myofascial pain with the 5-HT₃ receptor antagonist granisetron. A randomized and double-blind study.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2005-006042-41 |
| Trial protocol | SE |
| Global end of trial date | 31 December 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 01 May 2021 |
| First version publication date | 01 May 2021 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | NC3-project |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02230371 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Karolinska Institutet |
| Sponsor organisation address | 17177, Stockholm, Sweden, |
| Public contact | Department of Dental Medicine, Section for Orofacial Pain and Jaw Function, Karolinska Institutet, Karolinska Institutet, nikolaos.christidis@ki.se |
| Scientific contact | Department of Dental Medicine, Section for Orofacial Pain and Jaw Function, Karolinska Institutet, Karolinska Institutet, nikolaos.christidis@ki.se |

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 | 31 December 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 December 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The aim for the research project is to investigate if local treatment with granisetron reduces pain in patients with chronic craniomandibular myalgia.

Protection of trial subjects:

The study was approved by the regional ethical review board in Stockholm, Sweden (2006/192-31/4) and by the Medical Products Agency in Uppsala, Sweden (151:2006/7947). Adverse events were systematically collected during the study period.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 01 May 2006 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Sweden: 40 |
| Worldwide total number of subjects | 40 |
| EEA total number of subjects | 40 |

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) | 40 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Study was carried out at two centers, the specialist clinics for Orofacial Pain and Jaw Function, Department of Dental Medicine, Karolinska Institutet, Huddinge, Sweden and Clinical Oral Physiology at the Eastman Institute, Stockholm Public Dental Health (Folktandvården Stockholms län AB), Stockholm, Sweden, between May 2006 and December 2014.

Pre-assignment

Screening details:

437 patients were screened, 40 were eligible and included. Inclusion criteria: age ≥ 18 y, diagnosis of myofascial pain, duration of TMD-pain ≥ 3 months, self-assessed average M-TMD pain intensity ≥ 30 mm on a 100-mm VAS during one week prior to examination, pain upon digital palpation of the masseter and/or the temporalis muscles.

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 |

Blinding implementation details:

The study substances have identical appearance, smell and viscosity so both the patients and examiners were blinded to group assignment. A research assistant assigned the patients to treatment substance in consecutive order according to the randomization list, prepared the syringes and marked them with patient number. A numbered randomization list with the substances in random order in blocks of four was kept hidden to the examiners during the entire study.

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Granisetron |

Arm description:

Granisetron was used as active treatment.

The study comprised seven visits; V1) Screening for study participation and inclusion, V2-V4), Injection of study substances, and V5) Follow-ups at 1-month. Those patients in any group that still reported more than 30 % improvement at the 1-month visit follow-up were scheduled for follow-ups also after 2- (V6) and 6-months (V7).

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Granisetron |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Granisetron (KYTRIL®; 1 mg/mL, Roche, Stockholm, Sweden) was slowly injected into a maximum of six muscle sites in each patient. The most painful tender-points to palpation of the masticatory muscles were chosen, maximum 3 per muscle. The injected volume into each tender-point was 0.5 mL. Thus the maximum dose of granisetron a patient could receive was 3 mg per treatment.

| | |
|------------------|---------------------------|
| Arm title | Isotonic saline (placebo) |
|------------------|---------------------------|

Arm description:

Isotonic saline was used as control treatment. The study comprised seven visits; V1) Screening for study participation and inclusion, V2-V4), Injection of study substances, and V5) Follow-ups at 1-month. Those patients in any group that still reported more than 30 % improvement at the 1-month visit follow-up were scheduled for follow-ups also after 2- (V6) and 6-months (V7).

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|-------------------|
| Investigational medicinal product name | Isotonic saline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Isotonic saline (NaCl; 0.9 mg/mL, Fresenius Kabi, Uppsala, Sweden) was slowly injected into a maximum of six muscle sites in each patient. The most painful tender-points to palpation of the masticatory muscles were chosen, maximum 3 per muscle. The injected volume into each tender-point was 0.5 mL.

| Number of subjects in period 1 | Granisetron | Isotonic saline (placebo) |
|---------------------------------------|-------------|---------------------------|
| Started | 20 | 20 |
| Completed | 20 | 20 |

Baseline characteristics

Reporting groups

| | |
|---|---------------------------|
| Reporting group title | Granisetron |
| Reporting group description: | |
| Granisetron was used as active treatment. The study comprised seven visits; V1) Screening for study participation and inclusion, V2-V4), Injection of study substances, and V5) Follow-ups at 1-month. Those patients in any group that still reported more than 30 % improvement at the 1-month visit follow-up were scheduled for follow-ups also after 2- (V6) and 6-months (V7). | |
| Reporting group title | Isotonic saline (placebo) |
| Reporting group description: | |
| Isotonic saline was used as control treatment. The study comprised seven visits; V1) Screening for study participation and inclusion, V2-V4), Injection of study substances, and V5) Follow-ups at 1-month. Those patients in any group that still reported more than 30 % improvement at the 1-month visit follow-up were scheduled for follow-ups also after 2- (V6) and 6-months (V7). | |

| Reporting group values | Granisetron | Isotonic saline (placebo) | Total |
|--|-------------|---------------------------|-------|
| Number of subjects | 20 | 20 | 40 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 20 | 20 | 40 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 38.3 | 39.1 | |
| standard deviation | ± 15.1 | ± 16.1 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 18 | 19 | 37 |
| Male | 2 | 1 | 3 |
| Physical functioning | | | |
| Distribution of physical functioning assessed with the Graded Chronic Pain Scale (GCPS). | | | |
| Units: Subjects | | | |
| GCPS Grade 0 | 5 | 12 | 17 |
| GCPS Grade I | 4 | 1 | 5 |
| GCPS Grade II | 9 | 4 | 13 |
| GCPS Grade III | 0 | 1 | 1 |
| GCPS Grade IV | 1 | 1 | 2 |
| Missing value | 1 | 1 | 2 |

| | | | |
|---|-------|--------|---|
| Pain intensity | | | |
| Weekly pain intensity (VAS; 0–100 mm). Reported as median (IQR). | | | |
| Units: Score | | | |
| median | 52 | 57 | |
| standard deviation | ± 29 | ± 24 | - |
| Limitation in jaw function | | | |
| Limitation in jaw function assessed with the Jaw Disability Checklist (JDC). Reported as median (IQR). | | | |
| Units: Score (0-12) | | | |
| median | 3 | 2 | |
| standard deviation | ± 5 | ± 4 | - |
| MWO without pain | | | |
| Maximum voluntary mouth opening capacity (MVO) without pain. | | | |
| Units: mm | | | |
| arithmetic mean | 41.1 | 44.0 | |
| standard deviation | ± 9.3 | ± 10.9 | - |
| MWO with pain | | | |
| Maximum voluntary mouth opening capacity (MVO) with pain. | | | |
| Units: mm | | | |
| arithmetic mean | 49.7 | 52.8 | |
| standard deviation | ± 7.5 | ± 10.0 | - |

End points

End points reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Granisetron |
|-----------------------|-------------|

Reporting group description:

Granisetron was used as active treatment.

The study comprised seven visits; V1) Screening for study participation and inclusion, V2-V4), Injection of study substances, and V5) Follow-ups at 1-month. Those patients in any group that still reported more than 30 % improvement at the 1-month visit follow-up were scheduled for follow-ups also after 2- (V6) and 6-months (V7).

| | |
|-----------------------|---------------------------|
| Reporting group title | Isotonic saline (placebo) |
|-----------------------|---------------------------|

Reporting group description:

Isotonic saline was used as control treatment. The study comprised seven visits; V1) Screening for study participation and inclusion, V2-V4), Injection of study substances, and V5) Follow-ups at 1-month.

Those patients in any group that still reported more than 30 % improvement at the 1-month visit follow-up were scheduled for follow-ups also after 2- (V6) and 6-months (V7).

Primary: Pain intensity at 1, 2, 6 months

| | |
|-----------------|----------------------------------|
| End point title | Pain intensity at 1, 2, 6 months |
|-----------------|----------------------------------|

End point description:

Weekly pain intensity (VAS; 0–100 mm).

Reported as median (IQR).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

1, 2 and 6 months after repeated tender-point injections with Granisetron (active substance) or Isotonic saline (placebo).

| End point values | Granisetron | Isotonic saline (placebo) | | |
|-----------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: Score | | | | |
| median (standard deviation) | | | | |
| 1 month | 29 (± 41) | 29 (± 40) | | |
| 2 months | 32 (± 30) | 36 (± 25) | | |
| 6 months | 24 (± 35) | 34 (± 31) | | |

Statistical analyses

| | |
|----------------------------|-----------------------------------|
| Statistical analysis title | Difference Pain intensity 1 month |
|----------------------------|-----------------------------------|

Statistical analysis description:

Difference in pain intensity at 1 month between Granisetron and placebo.

| | |
|-------------------|---|
| Comparison groups | Granisetron v Isotonic saline (placebo) |
|-------------------|---|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

| | |
|--|---|
| Statistical analysis title | Difference Pain intensity 2 months |
| Statistical analysis description: Difference in pain intensity at 2 months between Granisetron and placebo. | |
| Comparison groups | Granisetron v Isotonic saline (placebo) |
| Number of subjects included in analysis | 40 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | = 0.009 |
| Method | Wilcoxon (Mann-Whitney) |

| | |
|--|---|
| Statistical analysis title | Difference Pain intensity 6 months |
| Statistical analysis description: Difference in pain intensity at 2 months between Granisetron and placebo. | |
| Comparison groups | Granisetron v Isotonic saline (placebo) |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.031 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Limitation in jaw function at 1, 2, 6 months

| | |
|--|--|
| End point title | Limitation in jaw function at 1, 2, 6 months |
| End point description: Limitation in jaw function assessed with the Jaw Disability Checklist (JDC). Reported as median (IQR). | |
| End point type | Secondary |
| End point timeframe: 1, 2 and 6 months after repeated tender-point injections with Granisetron (active substance) or Isotonic saline (placebo). | |

| End point values | Granisetron | Isotonic saline (placebo) | | |
|-----------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: Score | | | | |
| median (standard deviation) | | | | |
| 1 month | 3 (± 5) | 2 (± 4.5) | | |
| 2 months | 3 (± 4) | 2 (± 5.5) | | |
| 6 months | 3 (± 5) | 1 (± 3.5) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference Limitation in jaw function 1,2,6months |
|-----------------------------------|---|

Statistical analysis description:

Difference in limitation in jaw function at 1, 2 and 6 months between Granisetron and placebo.

| | |
|---|---|
| Comparison groups | Isotonic saline (placebo) v Granisetron |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: MWO without pain at 1, 2, 6 months

| | |
|-----------------|------------------------------------|
| End point title | MWO without pain at 1, 2, 6 months |
|-----------------|------------------------------------|

End point description:

Maximum voluntary mouth opening capacity (MVO) without pain.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1, 2 and 6 months after repeated tender-point injections with Granisetron (active substance) or Isotonic saline (placebo).

| End point values | Granisetron | Isotonic saline (placebo) | | |
|--------------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | | | | |
| 1 month | 42.9 (± 9.3) | 47.6 (± 9.4) | | |
| 2 months | 43.3 (± 9.4) | 46.9 (± 9.4) | | |
| 6 months | 47.2 (± 10.8) | 46.1 (± 6.2) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference MWO without pain 1, 2, 6 months |
| Statistical analysis description: Difference in MWO without pain at 1, 2 and 6 months between Granisetron and placebo. | |
| Comparison groups | Granisetron v Isotonic saline (placebo) |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: MWO with pain at 1, 2, 6 months

| | |
|--|---------------------------------|
| End point title | MWO with pain at 1, 2, 6 months |
| End point description: Maximum voluntary mouth opening capacity (MVO) with pain. | |
| End point type | Secondary |
| End point timeframe: 1, 2 and 6 months after repeated tender-point injections with Granisetron (active substance) or Isotonic saline (placebo). | |

| End point values | Granisetron | Isotonic saline (placebo) | | |
|--------------------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: Score (0-12) | | | | |
| arithmetic mean (standard deviation) | | | | |
| 1 month | 47.9 (± 8.2) | 52.8 (± 9.5) | | |
| 2 months | 49.2 (± 7.5) | 51.3 (± 9.8) | | |
| 6 months | 49.3 (± 10.5) | 50.4 (± 7.5) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Difference MWO with pain 1, 2, 6 months |
| Statistical analysis description: Difference in MWO with pain at 1, 2 and 6 months between Granisetron and placebo. | |
| Comparison groups | Granisetron v Isotonic saline (placebo) |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Physical functioning at 1 month

| | |
|-----------------|---------------------------------|
| End point title | Physical functioning at 1 month |
|-----------------|---------------------------------|

End point description:

Distribution of physical functioning assessed with the Graded Chronic Pain Scale (GCPS).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month after repeated tender-point injections with Granisetron (active substance) or Isotonic saline (placebo).

| End point values | Granisetron | Isotonic saline (placebo) | | |
|-----------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: Distribution | | | | |
| Grade 0 | 8 | 11 | | |
| Grade I | 6 | 1 | | |
| Grade II | 4 | 2 | | |
| Grade III | 1 | 3 | | |
| Grade IV | 1 | 0 | | |
| Missing value | 0 | 3 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Difference Physical functioning 1 month |
|----------------------------|---|

Statistical analysis description:

Difference in Physical functioning at 1 month between Granisetron and placebo.

| | |
|---|---|
| Comparison groups | Granisetron v Isotonic saline (placebo) |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Physical functioning at 2 months

| | |
|-----------------|----------------------------------|
| End point title | Physical functioning at 2 months |
|-----------------|----------------------------------|

End point description:

Distribution of physical functioning assessed with the Graded Chronic Pain Scale (GCPS).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

2 months after repeated tender-point injections with Granisetron (active substance) or Isotonic saline

(placebo).

| End point values | Granisetron | Isotonic saline (placebo) | | |
|-----------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: Distribution | | | | |
| Grade 0 | 7 | 6 | | |
| Grade I | 1 | 1 | | |
| Grade II | 3 | 1 | | |
| Grade III | 3 | 0 | | |
| Grade IV | 1 | 0 | | |
| Missing value | 5 | 12 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Difference Physical functioning 2 months |
| Statistical analysis description: Difference in Physical functioning at 2 months between Granisetron and placebo. | |
| Comparison groups | Granisetron v Isotonic saline (placebo) |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Physical functioning at 6 months

| | |
|---|----------------------------------|
| End point title | Physical functioning at 6 months |
| End point description: Distribution of physical functioning assessed with the Graded Chronic Pain Scale (GCPS). | |
| End point type | Secondary |
| End point timeframe: 6 months after repeated tender-point injections with Granisetron (active substance) or Isotonic saline (placebo). | |

| End point values | Granisetron | Isotonic saline (placebo) | | |
|-----------------------------|-----------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 20 | | |
| Units: Distribution | | | | |
| Grade 0 | 6 | 2 | | |
| Grade I | 1 | 2 | | |

| | | | | |
|---------------|----|----|--|--|
| Grade II | 1 | 1 | | |
| Grade III | 2 | 0 | | |
| Grade IV | 0 | 0 | | |
| Missing value | 10 | 15 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference Physical functioning at 6 months |
| Statistical analysis description: | |
| Difference in Physical functioning at 6 months between Granisetron and placebo. | |
| Comparison groups | Granisetron v Isotonic saline (placebo) |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The patients were asked to list any adverse events during the week following each injection.

Adverse event reporting additional description:

If any adverse event occurred the patients were asked to describe the event and to grade it as mild, moderate or severe. Only mild and short-lasting adverse events were reported after the first injections and no specific dictionary or frequency threshold was used.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|----------------------|
| Dictionary name | No specific was used |
|-----------------|----------------------|

| | |
|--------------------|-----|
| Dictionary version | n/a |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Granisetron and control |
|-----------------------|-------------------------|

Reporting group description: -

| Serious adverse events | Granisetron and control | | |
|---|-------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Granisetron and control | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | | |
| Gastrointestinal disorders | | | |
| Nausea, constipation, dizziness, hematoma and itching | Additional description: 4 patients in both groups reported mild, short lasting adverse events, such as nausea, constipation, dizziness, hematoma and itching after the first injection of substance. These adverse events did not occur after the second and third injections. | | |
| subjects affected / exposed | 4 / 40 (10.00%) | | |
| occurrences (all) | 4 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

| |
|---|
| The results are robust but a limited number of patients participated. The generalizability of the findings should also be investigated in other chronic pain disorders both local and generalized, such as work-related trapezius myalgia or fibromyalgi. |
|---|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26634569>