



## Clinical trial results:

## NEUROPHYSIOLOGIC STUDY AIMED AT EVALUATING ON EFFECT OF SATIVEX® ON SPASTICITY IN PROGRESSIVE MULTIPLE SCLEROSIS

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-002258-30 |
| Trial protocol           | IT             |
| Global end of trial date | 30 August 2013 |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 29 June 2016   |
| First version publication date | 02 August 2015 |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | M/SATIVX/01 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01538225 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Almirall S.A.   |
| Sponsor organisation address | General Mitre 151 , Barcelona, Spain,   |
| Public contact               | Global Medical Affairs, ALMIRALL S.A., 0034 932913490, carlos.vila@almirall.com |
| Scientific contact           | Global Medical Affairs, ALMIRALL S.A., 0034 932913490, carlos.vila@almirall.com |

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 November 2014 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 30 August 2013   |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 30 August 2013   |
| Was the trial ended prematurely?                     | No               |

Notes:

---

**General information about the trial**

---

Main objective of the trial:

To evaluate the effect of Sativex (THC:CBD 1:1 ratio oromucosal spray) compared to placebo in modifying neurophysiological measures of spasticity (H/M ratio scores at baseline and at week 4) in patients affected by lower limbs spasticity in Progressive Multiple Sclerosis

Protection of trial subjects:

Insurance policy available.

Informed consent and informative sheet for patients about study procedures.

Telephone contacts at weeks 2 and 8 for Sativex dose fixation.

Presential visits at weeks 0, 4, 6, 10.

Background therapy:

Approved antispastic medication

Evidence for comparator:

Not applicable, Placebo comparator

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 19 April 2012 |
| 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 | Italy: 44 |
| Worldwide total number of subjects   | 44        |
| EEA total number of subjects         | 44        |

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)                      | 43 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 1 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Following the protocol selection criteria

### Pre-assignment

Screening details:

Patients fulfilling the protocol selection criteria, including Sativex approved label requirements and providing informed consent. Subjects affected by Secondary or Primary-Progressive MS. Sativex has been gradually titrated. Subjects received in a random order each treatment (Sativex/Placebo) during 2 subsequent 4-weeks period divided by a washout

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 44 |
| Number of subjects completed | 44 |

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Overall trial (cross-over trial) (overall period) |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                           |
| Blinding used                | Double blind                                      |
| Roles blinded                | Subject, Investigator                             |

### Arms

|  |  |
|--|--|
| Are arms mutually exclusive?           | Yes  |
| <b>Arm title</b>                       | 4 weeks Sativex and 4 weeks Placebo              |
| Arm description: -                     |  |
| Arm type                               | Experimental                                     |
| Investigational medicinal product name | Sativex and Placebo                              |
| Investigational medicinal product code |  |
| Other name                             | THC:CDB oromucosal spray, Namiximols (USAN name) |
| Pharmaceutical forms                   | Oromucosal spray                                 |
| Routes of administration               | Oromucosal use                                   |

Dosage and administration details:

Spray containing, for 100 microliters, 2.7mg THC and 2.5mg CBD OR Placebo gradually titrated during the first 2 weeks of treatment, increasing the number of sprays until they reached and individualized sprayed dose (maximum 12 sprays)

|  |  |
|--|--|
| <b>Arm title</b>                       | 4 weeks Placebo and 4 weeks Sativex              |
| Arm description: -                     |  |
| Arm type                               | Experimental                                     |
| Investigational medicinal product name | Sativex and Placebo                              |
| Investigational medicinal product code |  |
| Other name                             | THC:CBD oromucosal spray, Namiximols (USAN name) |
| Pharmaceutical forms                   | Oromucosal spray                                 |
| Routes of administration               | Oromucosal use                                   |

Dosage and administration details:

Spray containing, for 100 microliters, 2.7mg THC and 2.5mg CBD OR Placebo gradually titrated during the first 2 weeks of treatment, increasing the number of sprays until they reached and individualized sprayed dose (maximum 12 sprays)

| <b>Number of subjects in period 1</b> | <b>4 weeks Sativex and<br/>4 weeks Placebo</b> | <b>4 weeks Placebo and<br/>4 weeks Sativex</b> |
|---------------------------------------|--|--|
| Started                               | 22   | 22   |
| Completed                             | 17   | 21   |
| Not completed                         | 5  | 1  |
| Adverse event, non-fatal              | 2  | -  |
| Intolerance to TMS                    | -  | 1  |
| Serious Adverse Event, non-fatal      | 1  | -  |
| Personal Reasons                      | 1  | -  |
| Starting neurorehabilitation          | 1  | -  |

## Baseline characteristics

### Reporting groups

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | 4 weeks Sativex and 4 weeks Placebo |
|-----------------------|-------------------------------------|

|                                |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | 4 weeks Placebo and 4 weeks Sativex |
|-----------------------|-------------------------------------|

|                                |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values | 4 weeks Sativex and<br>4 weeks Placebo | 4 weeks Placebo and<br>4 weeks Sativex | Total |
|------------------------|--|--|-------|
| Number of subjects     | 22                                     | 22                                     | 44    |
| Age categorical        |  |  |       |
| Units: Subjects        |  |  |       |
| Aged 18 years or above | 22                                     | 22                                     | 44    |
| Age continuous         |  |  |       |
| Units: years           |  |  |       |
| arithmetic mean        | 48.5                                   | 47.6                                   |       |
| standard deviation     | ± 7.8                                  | ± 8.4                                  | -     |
| Gender categorical     |  |  |       |
| Units: Subjects        |  |  |       |
| Female                 | 12                                     | 8                                      | 20    |
| Male                   | 10                                     | 14                                     | 24    |

## End points

### End points reporting groups

|                                |                                     |
|--------------------------------|-------------------------------------|
| Reporting group title          | 4 weeks Sativex and 4 weeks Placebo |
| Reporting group description: - |                                     |
| Reporting group title          | 4 weeks Placebo and 4 weeks Sativex |
| Reporting group description: - |                                     |

### Primary: The treatment effect on the H reflex/Motor response ratio (H/M ratio)

|   |   |
|---|---|
| End point title   | The treatment effect on the H reflex/Motor response ratio (H/M ratio) |
| End point description:  |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| H/M ratio scores at baseline and at week 4 for each treatment |   |

| End point values                     | 4 weeks Sativex and 4 weeks Placebo | 4 weeks Placebo and 4 weeks Sativex |  |  |
|--------------------------------------|-------------------------------------|-------------------------------------|--|--|
| Subject group type                   | Reporting group                     | Reporting group                     |  |  |
| Number of subjects analysed          | 15                                  | 19                                  |  |  |
| Units: H/M ratio value               |                                     |                                     |  |  |
| arithmetic mean (standard deviation) |                                     |                                     |  |  |
| Baseline sativex                     | 0.37 (± 0.19)                       | 0.3 (± 0.18)                        |  |  |
| After 4 weeks sativex treatment      | 0.34 (± 0.17)                       | 0.29 (± 0.16)                       |  |  |
| Baseline placebo                     | 0.31 (± 0.17)                       | 0.31 (± 0.18)                       |  |  |
| After 4 weeks placebo treatment      | 0.32 (± 0.18)                       | 0.29 (± 0.15)                       |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | H reflex/Motor response H/M ratio values evolution                        |
| Comparison groups                       | 4 weeks Sativex and 4 weeks Placebo v 4 weeks Placebo and 4 weeks Sativex |
| Number of subjects included in analysis | 34  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | equivalence <sup>[1]</sup>  |
| P-value                                 | = 0.405   |
| Method                                  | T-test  |

Notes:

[1] - There was no significant difference between change from baseline to week 4 in the H/M ratio score (p=0.405) under treatment with Sativex or placebo. No significant effect of sequence of treatment was observed

### Secondary: Resting Motor Thershold (RMT) at First Dorsal Interosseus (FDI)

|                                       |   |
|---------------------------------------|---|
| End point title                       | Resting Motor Thershold (RMT) at First Dorsal Interosseus (FDI) |
| End point description:                |   |
| End point type                        | Secondary   |
| End point timeframe:                  |   |
| From baseline to 4 weeks of treatment |   |

| End point values                     | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: RMT at FDI                    |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline Sativex                     | 60.71 (± 16.31)                           | 54.83 (± 12.45)                           |  |  |
| Week 4 Sativex                       | 61.14 (± 15.58)                           | 55.78 (± 14.79)                           |  |  |
| Baseline Placebo                     | 58.71 (± 13.73)                           | 54.26 (± 11.36)                           |  |  |
| Week 4 Placebo                       | 63.92 (± 13.77)                           | 54 (± 11.36)                              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Motor Evoked Potentials (MEP)

|  |                               |
|--|-------------------------------|
| End point title                        | Motor Evoked Potentials (MEP) |
| End point description:                 |                               |
| End point type                         | Secondary                     |
| End point timeframe:                   |                               |
| Frome baseline to 4 weeks of treatment |                               |

| End point values                     | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: MEP value evolution           |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline Sativex                     | 0.23 (± 0.15)                             | 0.32 (± 0.3)                              |  |  |
| week 4 Sativex                       | 0.24 (± 0.17)                             | 0.24 (± 0.16)                             |  |  |
| Baseline Placebo                     | 0.21 (± 0.1)                              | 0.26 (± 0.15)                             |  |  |



|                |                    |                    |  |  |
|----------------|--------------------|--------------------|--|--|
| Week 4 Placebo | 0.34 ( $\pm$ 0.42) | 0.24 ( $\pm$ 0.14) |  |  |
|----------------|--------------------|--------------------|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: MEP/Muscle potential ratios at APB and AH muscles evolution

|   |   |
|---|---|
| End point title   | MEP/Muscle potential ratios at APB and AH muscles evolution |
| End point description:<br>Motos Evoked Potentials (MEP)/ Muscles potentials ratios at APB (Abductor Pollicis Brevis) and AH (Abductor Hallucis) left (L) and right (R) muscles. |   |
| End point type  | Secondary   |
| End point timeframe:<br>From baseline to 4 weeks of treatment   |   |

| End point values                     | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: MEP/M                         |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline R APB Sativex               | 0.21 ( $\pm$ 0.1)                         | 0.23 ( $\pm$ 0.19)                        |  |  |
| Week 4 R APB Sativex                 | 0.21 ( $\pm$ 0.14)                        | 0.23 ( $\pm$ 0.17)                        |  |  |
| Baseline L APB Sativex               | 0.17 ( $\pm$ 0.13)                        | 0.23 ( $\pm$ 0.21)                        |  |  |
| Week 4 L APB Sativex                 | 0.2 ( $\pm$ 0.14)                         | 0.22 ( $\pm$ 0.21)                        |  |  |
| Baseline R AH Sativex                | 0.04 ( $\pm$ 0.02)                        | 0.06 ( $\pm$ 0.06)                        |  |  |
| Week 4 R AH Sativex                  | 0.05 ( $\pm$ 0.03)                        | 0.08 ( $\pm$ 0.08)                        |  |  |
| Baseline L AH Sativex                | 0.04 ( $\pm$ 0.02)                        | 0.06 ( $\pm$ 0.04)                        |  |  |
| Week 4 L AH Sativex                  | 0.04 ( $\pm$ 0.02)                        | 0.06 ( $\pm$ 0.04)                        |  |  |
| Baseline R APB Placebo               | 0.22 ( $\pm$ 0.13)                        | 0.23 ( $\pm$ 0.16)                        |  |  |
| Week 4 R APB Placebo                 | 0.19 ( $\pm$ 0.12)                        | 0.21 ( $\pm$ 0.15)                        |  |  |
| Baseline L APB Placebo               | 0.17 ( $\pm$ 0.14)                        | 0.22 ( $\pm$ 0.17)                        |  |  |
| Week 4 L APB Placebo                 | 0.19 ( $\pm$ 0.16)                        | 0.24 ( $\pm$ 0.19)                        |  |  |
| Baseline R AH Placebo                | 0.04 ( $\pm$ 0.02)                        | 0.06 ( $\pm$ 0.03)                        |  |  |
| Week 4 R AH Placebo                  | 0.04 ( $\pm$ 0.02)                        | 0.06 ( $\pm$ 0.03)                        |  |  |
| Baseline L AH Placebo                | 0.04 ( $\pm$ 0.02)                        | 0.05 ( $\pm$ 0.05)                        |  |  |
| Week 4 L AH Placebo                  | 0.04 ( $\pm$ 0.02)                        | 0.06 ( $\pm$ 0.07)                        |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Spasticity Modified Ashworth Scale (MAS)**

|                 |  |
|-----------------|--|
| End point title | Spasticity Modified Ashworth Scale (MAS) |
|-----------------|--|

End point description:

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

End point timeframe:

From baseline to 4 weeks of treatment

| End point values                     | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: MAS score evolution           |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline Sativex                     | 8.03 (± 4.26)                             | 6.79 (± 1.87)                             |  |  |
| Week 4 Sativex                       | 7.67 (± 4.53)                             | 6.37 (± 1.74)                             |  |  |
| Baseline Placebo                     | 7.4 (± 1.4)                               | 7 (± 1.63)                                |  |  |
| Week 4 Placebo                       | 7.33 (± 1.84)                             | 6.58 (± 2.01)                             |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Spasticity Numeric Rating Scale (NRS)**

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Spasticity Numeric Rating Scale (NRS) |
|-----------------|---------------------------------------|

End point description:

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

End point timeframe:

From baseline to 4 Weeks of treatment

| End point values                      | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|---------------------------------------|---|---|--|--|
| Subject group type                    | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed           | 15  | 19  |  |  |
| Units: Numeric Rating Scale evolution |   |   |  |  |
| arithmetic mean (standard deviation)  |   |   |  |  |
| Baseline Sativex                      | 7.27 (± 1.16)                             | 6.79 (± 1.87)                             |  |  |
| Week 4 Sativex                        | 6.73 (± 1.58)                             | 6.37 (± 1.74)                             |  |  |
| Baseline Placebo                      | 7.4 (± 1.4)                               | 7 (± 1.63)                                |  |  |
| Week 4 Placebo                        | 7.33 (± 1.84)                             | 6.58 (± 2.01)                             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Timed 10 meters walk

End point title Timed 10 meters walk

End point description:

End point type Secondary

End point timeframe:

From baseline to 4 weeks of treatment

| End point values                     | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: Seconds                       |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline Sativex                     | 39.5 (± 50.41)                            | 20.55 (± 15.55)                           |  |  |
| Week 4 Sativex                       | 34.99 (± 47.09)                           | 22.75 (± 19.36)                           |  |  |
| Baseline Placebo                     | 36.39 (± 47.74)                           | 22.63 (± 20.37)                           |  |  |
| Week 4 Placebo                       | 34.55 (± 43.44)                           | 22.48 (± 20.19)                           |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Nine Hole Peg Test (NHPT)

End point title Nine Hole Peg Test (NHPT)

End point description:

Upper extremity function test

End point type Secondary

End point timeframe:

From baseline to 4 weeks of treatment

| <b>End point values</b>              | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: NHPT scores evolution         |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline DH Sativex                  | 25.95 (± 5.54)                            | 25.66 (± 4.19)                            |  |  |
| Week 4 DH Sativex                    | 27.32 (± 7.77)                            | 24.94 (± 4.33)                            |  |  |
| Baseline NDH Sativex                 | 26.82 (± 3.99)                            | 30.26 (± 8.32)                            |  |  |
| Week 4 NDH Sativex                   | 25.02 (± 2.71)                            | 29.42 (± 7.99)                            |  |  |
| Baseline DH Placebo                  | 25.72 (± 6.51)                            | 27.47 (± 4.95)                            |  |  |
| Week 4 DH Placebo                    | 25.98 (± 7.37)                            | 26.02 (± 4.48)                            |  |  |
| Baseline NDH Placebo                 | 26.37 (± 4.19)                            | 31.73 (± 8.23)                            |  |  |
| Week 4 NDH Placebo                   | 24.42 (± 3.75)                            | 30.98 (± 9.37)                            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pain

|                                       |           |
|---------------------------------------|-----------|
| End point title                       | Pain      |
| End point description:                |           |
| End point type                        | Secondary |
| End point timeframe:                  |           |
| From baseline to 4 weeks of treatment |           |

| <b>End point values</b>              | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: 0-10 Numeric Rating Scale     |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline Sativex                     | 3.73 (± 3.22)                             | 3.16 (± 3.17)                             |  |  |
| Week 4 Sativex                       | 3.33 (± 3.15)                             | 2.63 (± 3)                                |  |  |
| Baseline Placebo                     | 4.4 (± 3.58)                              | 3.84 (± 3.35)                             |  |  |
| Week 4 Placebo                       | 3.47 (± 2.77)                             | 2 (± 2.69)                                |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Sleep Quality Numeric Rating Scale (NRS)

End point title Sleep Quality Numeric Rating Scale (NRS)

End point description:

End point type Secondary

End point timeframe:

From baseline to 4 weeks of treatment

| End point values                     | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: 0-10 Numeric Rating Scale     |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline Sativex                     | 2 ( $\pm$ 2.73)                           | 2.95 ( $\pm$ 2.97)                        |  |  |
| Week 4 Sativex                       | 1.33 ( $\pm$ 2.89)                        | 2.26 ( $\pm$ 3.19)                        |  |  |
| Baseline Placebo                     | 2.6 ( $\pm$ 3.02)                         | 4 ( $\pm$ 3.53)                           |  |  |
| Week 4 Placebo                       | 2.33 ( $\pm$ 3.24)                        | 2.37 ( $\pm$ 2.63)                        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Spasms

End point title Spasms

End point description:

End point type Secondary

End point timeframe:

From baseline to 4 weeks of treatment

| End point values                     | 4 weeks<br>Sativex and 4<br>weeks Placebo | 4 weeks<br>Placebo and 4<br>weeks Sativex |  |  |
|--------------------------------------|---|---|--|--|
| Subject group type                   | Reporting group                           | Reporting group                           |  |  |
| Number of subjects analysed          | 15  | 19  |  |  |
| Units: Spasms Frequency Score        |   |   |  |  |
| arithmetic mean (standard deviation) |   |   |  |  |
| Baseline Sativex                     | 5 ( $\pm$ 6.49)                           | 4.47 ( $\pm$ 6.5)                         |  |  |
| Week 4 Sativex                       | 4.28 ( $\pm$ 4.56)                        | 2.58 ( $\pm$ 4.84)                        |  |  |
| Baseline Placebo                     | 4.53 ( $\pm$ 3.85)                        | 5 ( $\pm$ 7.87)                           |  |  |

|                |                    |                 |  |  |
|----------------|--------------------|-----------------|--|--|
| Week 4 Placebo | 3.73 ( $\pm$ 4.13) | 3 ( $\pm$ 4.85) |  |  |
|----------------|--------------------|-----------------|--|--|

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected and reported during two subsequent 4-weeks periods divided by a 2-week washout. The overall duration for each patient was 10 weeks.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Adverse events |
|-----------------------|----------------|

Reporting group description: -

| Serious adverse events                            | Adverse events |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 1 / 43 (2.33%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |
| Gastrointestinal disorders                        |                |  |  |
| Pancreatitis acute                                |                |  |  |
| subjects affected / exposed                       | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |

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

| Non-serious adverse events                            | Adverse events   |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 22 / 43 (51.16%) |  |  |
| Vascular disorders                                    |                  |  |  |
| Hypotension   |                  |  |  |
| subjects affected / exposed                           | 2 / 43 (4.65%)   |  |  |
| occurrences (all)                                     | 2                |  |  |
| Hypertension  |                  |  |  |
| subjects affected / exposed                           | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                                     | 1                |  |  |
| Nervous system disorders                              |                  |  |  |

|   |                        |  |  |
|---|------------------------|--|--|
| Dizziness<br>subjects affected / exposed<br>occurrences (all)   | 10 / 43 (23.26%)<br>10 |  |  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)   | 2 / 43 (4.65%)<br>2    |  |  |
| General disorders and administration<br>site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)      | 1 / 43 (2.33%)<br>1    |  |  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 43 (2.33%)<br>1    |  |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Pharyngitis<br>subjects affected / exposed<br>occurrences (all)       | 1 / 43 (2.33%)<br>1    |  |  |
| Musculoskeletal and connective tissue<br>disorders<br>Muscular weakness<br>subjects affected / exposed<br>occurrences (all) | 4 / 43 (9.30%)<br>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**

None reported