



## Clinical trial results: Effect of oral CDP-choline on visual function in young amblyopic patients

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2006-006753-27  |
| Trial protocol           | IT              |
| Global end of trial date | 01 January 2017 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 29 April 2022 |
| First version publication date | 29 April 2022 |

### Trial information

#### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | 129/2006/O/Sper |
|-----------------------|-----------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |                                                                                                                   |
|------------------------------|-------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | TUBILUX PHARMA                                                                                                    |
| Sponsor organisation address | Via Costarica 20/22, Pomezia (RM), Italy, 00071                                                                   |
| Public contact               | Michela Fresina, Ophthalmology Unit<br>University of Bologna<br>Italy, +39 051 2142837, michela.fresina2@unibo.it |
| Scientific contact           | Fabio De Gregorio, Tubilux Pharma, +39 3386659374,<br>de_gregorio@tubilux.it                                      |

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? | Yes |
| 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                       | 01 January 2017  |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 01 December 2016 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 01 January 2017  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Verify whether oral administration of CDP-choline improves the visual function in amblyopic patients after 30-day treatment, as already observed after intramuscular administration of 500-1,000 mg of CDP-choline

Protection of trial subjects:

Informed consent signed by the parent and paper data collection in a supervised environment

Background therapy:

No previous treatment for amblyopia

No other local or systemic therapy

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 01 May 2006 |
| 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 | Italy: 67 |
| Worldwide total number of subjects   | 67        |
| EEA total number of subjects         | 67        |

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)                     | 67 |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Children suffering from anisometropic or strabismic amblyopia recruited from May 2006 to December 2006 in the Ophthalmology Service of the University of Bologna and the Eye Clinic of the Catholic University of Rome.

### Pre-assignment

Screening details:

Patients of both sexes suffering from anisometropic or strabismic monolateral amblyopia, aged between 5 and 10 years, not previously treated with conventional antiamblyopic therapies.

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 67 |
| Number of subjects completed | 67 |

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Visit 1 day 0           |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

### Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Treated patients |

Arm description:

Patients treated with CDP-choline (800 mg daily) + 2 h patching daily

|                                        |                                  |
|----------------------------------------|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Oral Cytidine-5'-diphosphocoline |
| Investigational medicinal product code |                                  |
| Other name                             | CITICOLINE                       |
| Pharmaceutical forms                   | Granules                         |
| Routes of administration               | Oral use                         |

Dosage and administration details:

7-28 mg/Kg/daily

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Control Group |
|------------------|---------------|

Arm description:

Patients treated with 2 h patching daily

|                                                           |                |
|-----------------------------------------------------------|----------------|
| Arm type                                                  | Adhesive patch |
| No investigational medicinal product assigned in this arm |                |

| Number of subjects in period 1 | Treated patients | Control Group |
|--------------------------------|------------------|---------------|
| Started                        | 37               | 30            |
| Completed                      | 37               | 30            |

## Period 2

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | Visit 2 day 30          |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

## Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Treated patients |

Arm description:

Patients treated with CDP-choline (800 mg daily) + 2 h patching daily

|                                        |                                  |
|----------------------------------------|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Oral Cytidine-5'-diphosphocoline |
| Investigational medicinal product code |                                  |
| Other name                             | CITICOLINE                       |
| Pharmaceutical forms                   | Granules                         |
| Routes of administration               | Oral use                         |

Dosage and administration details:

7-28 mg/Kg/daily

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Control Group |
|------------------|---------------|

Arm description:

Patients treated with 2 h patching daily

|                                                           |                |
|-----------------------------------------------------------|----------------|
| Arm type                                                  | Adhesive patch |
| No investigational medicinal product assigned in this arm |                |

| Number of subjects in period 2 | Treated patients | Control Group |
|--------------------------------|------------------|---------------|
| Started                        | 37               | 30            |
| Completed                      | 37               | 30            |

**Period 3**

|                              |                         |
|------------------------------|-------------------------|
| Period 3 title               | Visit 3 day 90          |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

**Arms**

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Treated patients |

Arm description:

Patients treated with CDP-choline (800 mg daily) + 2 h patching daily

|                                        |                                  |
|----------------------------------------|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Oral Cytidine-5'-diphosphocoline |
| Investigational medicinal product code |                                  |
| Other name                             | CITICOLINE                       |
| Pharmaceutical forms                   | Granules                         |
| Routes of administration               | Oral use                         |

Dosage and administration details:

7-28 mg/Kg/daily

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Control Group |
|------------------|---------------|

Arm description:

Patients treated with 2 h patching daily

|                                                           |                |
|-----------------------------------------------------------|----------------|
| Arm type                                                  | Adhesive patch |
| No investigational medicinal product assigned in this arm |                |

| <b>Number of subjects in period 3</b>            | Treated patients | Control Group |
|--------------------------------------------------|------------------|---------------|
| Started                                          | 37               | 30            |
| Completed                                        | 32               | 29            |
| Not completed                                    | 5                | 1             |
| Drop out for reasons no related to the treatment | 5                | 1             |

## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Treated patients |
|-----------------------|------------------|

Reporting group description:

Patients treated with CDP-choline (800 mg daily) + 2 h patching daily

|                       |               |
|-----------------------|---------------|
| Reporting group title | Control Group |
|-----------------------|---------------|

Reporting group description:

Patients treated with 2 h patching daily

| Reporting group values | Treated patients | Control Group | Total |
|------------------------|------------------|---------------|-------|
| Number of subjects     | 37               | 30            | 67    |
| Age categorical        |                  |               |       |
| Units: Subjects        |                  |               |       |
| Children (2-11 years)  | 37               | 30            | 67    |
| Age continuous         |                  |               |       |
| Units: years           |                  |               |       |
| arithmetic mean        | 5.9              | 6.2           |       |
| full range (min-max)   | 5 to 10          | 5 to 10       | -     |
| Gender categorical     |                  |               |       |
| Units: Subjects        |                  |               |       |
| Female                 | 21               | 16            | 37    |
| Male                   | 16               | 14            | 30    |

## End points

### End points reporting groups

|                                                                                                       |                  |
|-------------------------------------------------------------------------------------------------------|------------------|
| Reporting group title                                                                                 | Treated patients |
| Reporting group description:<br>Patients treated with CDP-choline (800 mg daily) + 2 h patching daily |                  |
| Reporting group title                                                                                 | Control Group    |
| Reporting group description:<br>Patients treated with 2 h patching daily                              |                  |
| Reporting group title                                                                                 | Treated patients |
| Reporting group description:<br>Patients treated with CDP-choline (800 mg daily) + 2 h patching daily |                  |
| Reporting group title                                                                                 | Control Group    |
| Reporting group description:<br>Patients treated with 2 h patching daily                              |                  |
| Reporting group title                                                                                 | Treated patients |
| Reporting group description:<br>Patients treated with CDP-choline (800 mg daily) + 2 h patching daily |                  |
| Reporting group title                                                                                 | Control Group    |
| Reporting group description:<br>Patients treated with 2 h patching daily                              |                  |

### Primary: Change in visual acuity (BCVA) of amblyopic eyes measured by Snellen's E chart

|                                                                                                                                                                                                                              |                                                                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                              | Change in visual acuity (BCVA) of amblyopic eyes measured by Snellen's E chart |
| End point description:                                                                                                                                                                                                       |                                                                                |
| End point type                                                                                                                                                                                                               | Primary                                                                        |
| End point timeframe:<br>Data were collected in 3 time points:<br>Visit 1: baseline data were collected<br>Visit 2: after 30 days of treatment<br>Visit 3: after 90 days (the treatment was discontinued in the last 60 days) |                                                                                |

| End point values                     | Treated patients | Control Group   | Treated patients | Control Group   |
|--------------------------------------|------------------|-----------------|------------------|-----------------|
| Subject group type                   | Reporting group  | Reporting group | Reporting group  | Reporting group |
| Number of subjects analysed          | 37               | 30              | 37               | 30              |
| Units: LogMAR                        |                  |                 |                  |                 |
| arithmetic mean (standard deviation) | 0.34 (± 0.22)    | 0.26 (± 0.19)   | 0.16 (± 0.15)    | 0.09 (± 0.09)   |

| End point values | Treated patients | Control Group |  |  |
|------------------|------------------|---------------|--|--|
|------------------|------------------|---------------|--|--|

|                                      |                    |                    |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 32                 | 29                 |  |  |
| Units: LogMAR                        |                    |                    |  |  |
| arithmetic mean (standard deviation) | 0.14 ( $\pm$ 0.15) | 0.13 ( $\pm$ 0.15) |  |  |

## Statistical analyses

|                                         |                                                                                                        |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Two-way ANOVA                                                                                          |
| Comparison groups                       | Treated patients v Treated patients v Control Group v Treated patients v Control Group v Control Group |
| Number of subjects included in analysis | 195                                                                                                    |
| Analysis specification                  | Pre-specified                                                                                          |
| Analysis type                           | superiority                                                                                            |
| P-value                                 | < 0.05                                                                                                 |
| Method                                  | ANOVA                                                                                                  |

|                                         |                                                                     |
|-----------------------------------------|---------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Tukey's test                                                        |
| Comparison groups                       | Control Group v Treated patients v Control Group v Treated patients |
| Number of subjects included in analysis | 128                                                                 |
| Analysis specification                  | Pre-specified                                                       |
| Analysis type                           | superiority                                                         |
| P-value                                 | < 0.05                                                              |
| Method                                  | Tukey's test                                                        |

## Secondary: BCVA of healthy eyes measured by isolated E letters (Snellen's E chart)

|                 |                                                                         |
|-----------------|-------------------------------------------------------------------------|
| End point title | BCVA of healthy eyes measured by isolated E letters (Snellen's E chart) |
|-----------------|-------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Data were collected in 3 time points:

Visit 1: baseline data were collected

Visit 2: after 30 days of treatment

Visit 3: after 90 days (the treatment was discontinued in the last 60 days)



| End point values                     | Treated patients   | Control Group      | Treated patients   | Control Group      |
|--------------------------------------|--------------------|--------------------|--------------------|--------------------|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group    | Reporting group    |
| Number of subjects analysed          | 37                 | 30                 | 37                 | 30                 |
| Units: LogMAR                        |                    |                    |                    |                    |
| arithmetic mean (standard deviation) | 0.07 ( $\pm$ 0.09) | 0.02 ( $\pm$ 0.06) | 0.04 ( $\pm$ 0.06) | 0.01 ( $\pm$ 0.02) |

| End point values                     | Treated patients   | Control Group      |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 32                 | 29                 |  |  |
| Units: LogMAR                        |                    |                    |  |  |
| arithmetic mean (standard deviation) | 0.04 ( $\pm$ 0.08) | 0.01 ( $\pm$ 0.02) |  |  |

### Statistical analyses

| Statistical analysis title              | Two-way ANOVA                                                                                          |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Treated patients v Control Group v Treated patients v Control Group v Treated patients v Control Group |
| Number of subjects included in analysis | 195                                                                                                    |
| Analysis specification                  | Pre-specified                                                                                          |
| Analysis type                           | superiority                                                                                            |
| P-value                                 | < 0.05                                                                                                 |
| Method                                  | ANOVA                                                                                                  |

| Statistical analysis title              | Tukey's test                                                        |
|-----------------------------------------|---------------------------------------------------------------------|
| Comparison groups                       | Treated patients v Control Group v Treated patients v Control Group |
| Number of subjects included in analysis | 128                                                                 |
| Analysis specification                  | Pre-specified                                                       |
| Analysis type                           | superiority                                                         |
| P-value                                 | < 0.05                                                              |
| Method                                  | Tukey's test                                                        |

### Secondary: BCVA of amblyopic eyes measured by isolated E letters

|                        |                                                       |
|------------------------|-------------------------------------------------------|
| End point title        | BCVA of amblyopic eyes measured by isolated E letters |
| End point description: |                                                       |

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

End point timeframe:

Data were collected in 3 time points:

Visit 1: baseline data were collected

Visit 2: after 30 days of treatment

| <b>End point values</b>              | Treated patients   | Control Group      | Treated patients   | Control Group      |
|--------------------------------------|--------------------|--------------------|--------------------|--------------------|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group    | Reporting group    |
| Number of subjects analysed          | 37                 | 30                 | 37                 | 30                 |
| Units: LogMAR                        |                    |                    |                    |                    |
| arithmetic mean (standard deviation) | 0.21 ( $\pm$ 0.26) | 0.17 ( $\pm$ 0.21) | 0.08 ( $\pm$ 0.14) | 0.03 ( $\pm$ 0.08) |

| <b>End point values</b>              | Treated patients   | Control Group      |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 32                 | 29                 |  |  |
| Units: LogMAR                        |                    |                    |  |  |
| arithmetic mean (standard deviation) | 0.05 ( $\pm$ 0.12) | 0.06 ( $\pm$ 0.13) |  |  |

### Statistical analyses

| <b>Statistical analysis title</b>       | Two-way ANOVA                                                                                          |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Treated patients v Control Group v Treated patients v Control Group v Treated patients v Control Group |
| Number of subjects included in analysis | 195                                                                                                    |
| Analysis specification                  | Pre-specified                                                                                          |
| Analysis type                           | superiority                                                                                            |
| P-value                                 | < 0.05                                                                                                 |
| Method                                  | ANOVA                                                                                                  |

| <b>Statistical analysis title</b>       | Tukey's test                                                        |
|-----------------------------------------|---------------------------------------------------------------------|
| Comparison groups                       | Treated patients v Control Group v Treated patients v Control Group |
| Number of subjects included in analysis | 128                                                                 |
| Analysis specification                  | Pre-specified                                                       |
| Analysis type                           | superiority                                                         |
| P-value                                 | < 0.05                                                              |
| Method                                  | Tukey's test                                                        |

## Adverse events

---

### Adverse events information<sup>[1]</sup>

---

Timeframe for reporting adverse events:

Throughout the entire timeframe of the trial.

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

---

### Dictionary used

---

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

---

|                    |     |
|--------------------|-----|
| Dictionary version | 9.1 |
|--------------------|-----|

---

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

---

#### 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 adverse reaction to CDP-choline, either minor or serious, was reported throughout the trial. The safety of the treatment was judged to be excellent by the investigators.

## 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