



## Clinical trial results:

### A Phase II Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy, Safety, and Tolerability of Arbaclofen Administered for the Treatment of Social Function in Children and Adolescents with Autism Spectrum Disorders.

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2018-000942-21  |
| Trial protocol           | GB              |
| Global end of trial date | 27 January 2023 |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 20 June 2026  |
| First version publication date    | 20 June 2026  |
| Summary attachment (see zip file) | SUMMARY (AIMS2-CT1_CLINICAL STUDY REPORT SUMMARY_apr2026.pdf)<br>primary paper (parellada et al_2026_efficacy, safety and tolerability of arbaclofen_AIMS-2-TRIALS-CT1.pdf) |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | AIMS-2-CT1 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03682978 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Hospital General Universitario Gregorio Marañón   |
| Sponsor organisation address | C/ Dr Esquerdo 46, Madrid, Spain, 28007   |
| Public contact               | Professor Andre Strydom, Institute of Psychiatry, Psychology and Neuroscience, King's College London, +44 7894551353, andre.strydom@kcl.ac.uk |
| Scientific contact           | Professor Andre Strydom, Institute of Psychiatry, Psychology and Neuroscience, King's College London, +34 914265006, carango@hggm.es          |

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                       | 27 January 2024 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 27 January 2023 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 27 January 2023 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The overall goal of this project is to improve patient outcomes. For this study the primary objective is to examine the effect of Arbaclofen compared to placebo on social function in children and adolescents (age 5 - 17) with Autism spectrum disorders.

Protection of trial subjects:

Patients were protected by being treated by professional and experienced clinicians and research workers. The protocol was followed at all times and when protocol procedures were difficult or strenuous, the study teams and clinical teams have provided breaks and reassurance. If patients did not want particular protocol procedures (such as blood taking) they were not included in the study. If patients showed resistance after initially providing assent, this was handled according to good practice, and either the procedures were stopped and the patient excluded, or the patient was sufficiently reassured and calm when proceeding.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 01 November 2018 |
| 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 | United Kingdom: 25 |
| Country: Number of subjects enrolled | France: 22         |
| Country: Number of subjects enrolled | Spain: 77          |
| Worldwide total number of subjects   | 124                |
| EEA total number of subjects         | 99                 |

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)                    | 54 |
| Adolescents (12-17 years)                | 70 |
| Adults (18-64 years)                     | 0  |
| From 65 to 84 years                      | 0  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

FPFV: 19Sep20219

LPLV: 27Jan2023

### Pre-assignment

Screening details:

18 patients were screen failures or discontinued before randomization

- COVID restrictions government (n=1)
- Participant requested to discontinue (n=4)
- Screening failure, patient does not meet all in-exclusion criteria (n=12)
- Rescreening (n=1)

### 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, Monitor, Data analyst, Carer, Assessor |

Blinding implementation details:

all study team members dealing directly with the subject were blinded, as was the subject. the only person not blinded was the pharmacist handing out the medication, and the unblinded monitor, checking randomisation procedures.

### Arms

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | placebo and arbaclofen |
|------------------|------------------------|

Arm description:

reporting both arms together

|  |            |
|--|------------|
| Arm type                               | combined   |
| Investigational medicinal product name | arbaclofen |
| Investigational medicinal product code |            |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

orally disintegrating tabs, round, white and bevelled edges

placebo:

0mg

arbaclofen:

5mg, 10mg, 15mg and 20mg

| <b>Number of subjects in period 1<sup>[1]</sup></b> | placebo and arbaclofen |
|---|------------------------|
| Started   | 123                    |
| Completed   | 116                    |
| Not completed                                       | 7                      |
| Physician decision                                  | 1                      |

|                    |   |
|--------------------|---|
| too stressful      | 2 |
| other              | 1 |
| Lost to follow-up  | 2 |
| Protocol deviation | 1 |

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Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: During the study, a number of participants were identified as screening failures. Hence the number of subjects in the baseline period is not equal to the worldwide number enrolled in the trial.

## Baseline characteristics

### Reporting groups

|                                |               |
|--------------------------------|---------------|
| Reporting group title          | overall trial |
| Reporting group description: - |               |

| Reporting group values    | overall trial | Total |  |
|---------------------------|---------------|-------|--|
| Number of subjects        | 123           | 123   |  |
| Age categorical           |               |       |  |
| Units: Subjects           |               |       |  |
| Adolescents (12-17 years) | 66            | 66    |  |
| Children (5-11)           | 57            | 57    |  |
| Age continuous            |               |       |  |
| Units: years              |               |       |  |
| arithmetic mean           | 12            |       |  |
| standard deviation        | ± 3.2         | -     |  |
| Gender categorical        |               |       |  |
| Units: Subjects           |               |       |  |
| Female                    | 102           | 102   |  |
| Male                      | 21            | 21    |  |

### Subject analysis sets

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | primary endpoint   |
| Subject analysis set type  | Intention-to-treat |

Subject analysis set description:

A total of 59 ITT patients in arbaclofen vs 63 in placebo were analysed. The Socialization domain of the Vineland-3 was chosen as the primary outcome. We, therefore, explored changes after treatment in each treatment arm for the Socialization Standard score (with mean 100 and standard deviation 15 – Table 11.4.1-1) and the average of its three subdomains (i.e. play and leisure, social skills and interpersonal relationships – Table 11.4.1-2) Growth Scale Values.

| Reporting group values    | primary endpoint |  |  |
|---------------------------|------------------|--|--|
| Number of subjects        | 122              |  |  |
| Age categorical           |                  |  |  |
| Units: Subjects           |                  |  |  |
| Adolescents (12-17 years) | 66               |  |  |
| Children (5-11)           | 57               |  |  |
| Age continuous            |                  |  |  |
| Units: years              |                  |  |  |
| arithmetic mean           | 12               |  |  |
| standard deviation        | ± 3.2            |  |  |
| Gender categorical        |                  |  |  |
| Units: Subjects           |                  |  |  |
| Female                    | 102              |  |  |
| Male                      | 20               |  |  |

## End points

### End points reporting groups

|  |                        |
|--|------------------------|
| Reporting group title  | placebo and arbaclofen |
| Reporting group description:<br>reporting both arms together   |                        |
| Subject analysis set title   | primary endpoint       |
| Subject analysis set type  | Intention-to-treat     |
| Subject analysis set description:<br>A total of 59 ITT patients in arbaclofen vs 63 in placebo were analysed. The Socialization domain of the Vineland-3 was chosen as the primary outcome. We, therefore, explored changes after treatment in each treatment arm for the Socialization Standard score (with mean 100 and standard deviation 15 – Table 11.4.1-1) and the average of its three subdomains (i.e. play and leisure, social skills and interpersonal relationships – Table 11.4.1-2) Growth Scale Values. |                        |

### Primary: Vineland Socialization Standard Score

|   |  |
|---|--|
| End point title   | Vineland Socialization Standard Score <sup>[1]</sup> |
| End point description:  |  |
| End point type  | Primary  |
| End point timeframe:<br>standard score of the socialization domain, adjusting for baseline, age, sex and site |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The statistical analysis corresponding to this part of the results is clearly described in the paper - Parellada et al, 2026 doi: 10.1016/j.eclnm.2026.103760

| End point values                     | placebo and arbaclofen | primary endpoint     |  |  |
|--------------------------------------|------------------------|----------------------|--|--|
| Subject group type                   | Reporting group        | Subject analysis set |  |  |
| Number of subjects analysed          | 122                    | 122                  |  |  |
| Units: number                        |                        |                      |  |  |
| arithmetic mean (standard deviation) | 72 (± 18)              | 72 (± 18)            |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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

Timeframe for reporting adverse events:

overall trial

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 21 |
|--------------------|----|

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | arbaclofen |
|-----------------------|------------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events                            | arbaclofen     | Placebo        |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 49 (0.00%) | 0 / 63 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

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

| Non-serious adverse events                            | arbaclofen     | Placebo        |  |
|---|----------------|----------------|--|
| Total subjects affected by non-serious adverse events |                |                |  |
| subjects affected / exposed                           | 0 / 49 (0.00%) | 0 / 63 (0.00%) |  |

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: The adverse events corresponding to these results are clearly described in the paper - Parellada et al, 2026 doi: 10.1016/j.eclinm.2026.103760



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 17 September 2019 | substantial amendment #1 - protocol 4.0<br>various administrative changes  |
| 04 February 2020  | substantial amendment #2 - protocol 5.0<br>extension expiry date medication  |
| 02 September 2020 | substantial amendment #3 - protocol 6.0<br>remote assessments  |
| 16 November 2020  | substantial amendment #4 - protocol 7.1<br>adding digital biomarkers   |
| 23 February 2021  | substantial amendment #5 - protocol 7.2<br>1) in the protocol, tables 4.1-1, 4.1-2 and appendix 5 have been corrected to indicate that the collection of the digital biomarkers equipment will be done on visit 7 (and not 8)<br>2) This change has also been reflected in the consent form for parents and +18 (figure)<br>3) in the protocol, we have substituted San Sebastian for the centres in Castille-Leon |
| 19 April 2022     | non-substantial amendment #6 to extend recruitment - protocol v9.0 - approved by Spain   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date          | Interruption | Restart date |
|---------------|--------------|--------------|
| 13 March 2020 | Corona       | -            |

Notes:

### Limitations and caveats

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

Efficacy results have yielded mixed results. We hypothesized that treatment with arbaclofen would improve social function as measured with the Vineland-3 Socialization domain. Our results, however, show that both arbaclofen and placebo-treated patients

Notes: