



Clinical trial results:

The effect of curcumin and genistein in CF patients with a class III mutation

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-000817-30 |
| Trial protocol | NL |
| Global end of trial date | 08 May 2015 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 11 March 2020 |
| First version publication date | 11 March 2020 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | TICTAC-2014 |
|-----------------------|-------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UMC Utrecht |
| Sponsor organisation address | Lundlaan 6, Utrecht, Netherlands, |
| Public contact | Prof. dr. C.K. van der Ent, University Medical Center Utrecht, 0031 (0)887553201, k.vanderent@umcutrecht.nl |
| Scientific contact | Gitte Berkers, University Medical Center Utrecht, 0031 (0)887553741, g.berkers-3@umcutrecht.nl |

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 | 01 November 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 May 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 May 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Curcumin and genistein might be a cheap alternative for treating patients with a class III gating mutation

Main objective of the trial is to investigate the clinical response on treatment with curcumin and genistein in CF-patients with a class III S1251N mutation.

Protection of trial subjects:

N.A.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 18 September 2014 |
| 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 | Netherlands: 13 |
| Worldwide total number of subjects | 13 |
| EEA total number of subjects | 13 |

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) | 4 |
| Adolescents (12-17 years) | 4 |
| Adults (18-64 years) | 5 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

inclusion criteria:

- CFTR genotype compound/ S1251N
- Already had a rectal biopsy to produce an organoid
- Male and female patients, aged 6 years or older on the date of informed consent or, where appropriate, date of assent
- Signed informed consent form (IC), and where appropriate, signed assent form

Period 1

| | |
|------------------------------|-----------------------------------|
| Period 1 title | treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | No |
| Arm title | Treatment |

Arm description:

treatment with curcumin and genistein

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | curcumin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

curcumin was dosed based on the weight of the patient with a minimum dose of 102.9 and maximum dose of 138.5 mg/Kg/day

| | |
|--|-----------|
| Investigational medicinal product name | genistein |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Dose was based on weight with a minimum dose of 3.3 and a maximum dose of 4.8 mg/Kg/day

| | |
|------------------|----------|
| Arm title | baseline |
|------------------|----------|

Arm description: -

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

| Number of subjects in period 1 | Treatment | baseline |
|---------------------------------------|-----------|----------|
| Started | 13 | 13 |
| Completed | 13 | 13 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | treatment period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values | treatment period | Total | |
|---|------------------|-------|--|
| Number of subjects | 13 | 13 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 15.0 | | |
| inter-quartile range (Q1-Q3) | 10.0 to 33.0 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 5 | |
| Male | 8 | 8 | |

End points

End points reporting groups

| | |
|---|-----------|
| Reporting group title | Treatment |
| Reporting group description: treatment with curcumin and genistein | |
| Reporting group title | baseline |
| Reporting group description: - | |

Primary: Sweat chloride concentration

| | |
|--|------------------------------|
| End point title | Sweat chloride concentration |
| End point description: | |
| End point type | Primary |
| End point timeframe: after 8 weeks of treatment | |

| End point values | Treatment | baseline | | |
|---------------------------------------|-----------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 13 | | |
| Units: mmol/L | | | | |
| median (inter-quartile range (Q1-Q3)) | 76 (64 to 81) | 80.0 (65.5 to 91.0) | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Wilcoxon signed rank test |
| Comparison groups | baseline v Treatment |
| Number of subjects included in analysis | 26 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (final values) |
| Point estimate | 30 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 18.28 |
| upper limit | 41.72 |
| Variability estimate | Standard deviation |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first visit of the trial (t=0) until the last visit (t= 8weeks)

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|----|
| Dictionary name | NA |
|-----------------|----|

| | |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | treatment period |
|-----------------------|------------------|

Reporting group description:

during treatment with curcumin and genistein

| Serious adverse events | treatment period | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | treatment period | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 13 (92.31%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | | |
| occurrences (all) | 5 | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Night sweats | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | | |
| Gastrointestinal disorders | | | |
| Yellow stool | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | | |
| occurrences (all) | 4 | | |
| Flatulence | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | | |
| occurrences (all) | 3 | | |
| stomach ache | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | | |
| occurrences (all) | 7 | | |
| diarrhea | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| throwing up | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |
| cough up more sputum | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 27 June 2014 | The effect of curcumin and genistein was evaluated but not compared to the effect of Ivacaftor treatment. This was done in a separate trial |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported