



Clinical trial results:

The effects of melatonin treatment on bone, marrow, sleep and arterial stiffness in postmenopausal women

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2020-002934-34 |
| Trial protocol | DK |
| Global end of trial date | 01 February 2022 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 24 May 2023 |
| First version publication date | 24 May 2023 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 2020-AKA |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04864509 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Aarhus University Hospital |
| Sponsor organisation address | Palle Juul-Jensens Boulevard 99, Aarhus N, Denmark, 8200 |
| Public contact | Klinik for knogleskørhed, Anne Kristine Amstrup, anneamst@rm.dk |
| Scientific contact | Klinik for knogleskørhed, Anne Kristine Amstrup, anneamst@rm.dk |

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 February 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 February 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 February 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Changes in gene expression in mesenchymal stem cells

Protection of trial subjects:

At every visit the participants were asked whether or not they had experienced adverse event to the treatment.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 23 May 2021 |
| 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 | Denmark: 41 |
| Worldwide total number of subjects | 41 |
| EEA total number of subjects | 41 |

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) | 22 |
| From 65 to 84 years | 19 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were invited by letter. Recruitment period was from May to September 2021

Pre-assignment

Screening details:

Participants responding positively to the invitation received a questionnaire regarding exclusion criteria. Those who did not fulfill the exclusions criteria received further information about the study. They were further invited to an interview at the study place.

Period 1

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

Blinding implementation details:

Glostrup Pharmacy randomized the participants (using a computer) into blocks of 2,4, and 8 participants. The block-sizes were unknown to the investigators. The participants as well as the investigators were blinded to the study drug allocation

Arms

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

Arm description:

Nightly dose og 10mg melatonin

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | melatonin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg nightly

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo

| | |
|--|---------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

10 mg nightly

| Number of subjects in period 1 | Melatonin | Placebo |
|---------------------------------------|-----------|---------|
| Started | 21 | 20 |
| Completed | 19 | 20 |
| Not completed | 2 | 0 |
| Adverse event, non-fatal | 1 | - |
| Illness in the nearby family | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Overall period trial |
|-----------------------|----------------------|

Reporting group description: -

| Reporting group values | Overall period trial | Total | |
|---|----------------------|-------|--|
| Number of subjects | 41 | 41 | |
| Age categorical | | | |
| Mean age | | | |
| 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 | | | |
| melatonin group: 63 (56-74) placebo group: 64 (55-75) | | | |
| Units: years | | | |
| arithmetic mean | 64 | | |
| inter-quartile range (Q1-Q3) | 55 to 74 | - | |
| Gender categorical | | | |
| Postmenopausal women | | | |
| Units: Subjects | | | |
| Female | 41 | 41 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|--------------------------------|-----------|
| Reporting group title | Melatonin |
| Reporting group description: | |
| Nightly dose og 10mg melatonin | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo | |

Primary: Changes in mesenchymal stem cells

| | |
|---|-----------------------------------|
| End point title | Changes in mesenchymal stem cells |
| End point description: | |
| data still being analyzed | |
| End point type | Primary |
| End point timeframe: | |
| Changes after three months of treatment | |

| End point values | Melatonin | Placebo | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 16 | | |
| Units: percent | | | | |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | T-test |
| Comparison groups | Melatonin v Placebo |
| Number of subjects included in analysis | 29 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 2-sided |
| Parameter estimate | Median difference (final values) |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| Variability estimate | Standard deviation |

Secondary: Changes in 24H blood pressure

| | |
|--|-------------------------------|
| End point title | Changes in 24H blood pressure |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Changes before and after three months of treatment | |

| End point values | Melatonin | Placebo | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 19 | | |
| Units: percent | | | | |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in arterial stiffness

| | |
|---|-------------------------------|
| End point title | Changes in arterial stiffness |
| End point description: data still being analyzed | |
| End point type | Secondary |
| End point timeframe: | |
| Changes before and after three months of treatment | |

| End point values | Melatonin | Placebo | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 19 | | |
| Units: percent | | | | |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: changes in biochemical parameters

| | |
|---|-----------------------------------|
| End point title | changes in biochemical parameters |
| End point description: data still being analyzed | |
| End point type | Secondary |

End point timeframe:

Changes before and after three months of treatment

| End point values | Melatonin | Placebo | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: Percent | | | | |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in BMD

| | |
|--|----------------|
| End point title | Changes in BMD |
| End point description: | |
| Data still being analyzed | |
| End point type | Secondary |
| End point timeframe: | |
| Changes before and after three months of treatment | |

| End point values | Melatonin | Placebo | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: percent | | | | |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in quality of sleep

| | |
|--|-----------------------------|
| End point title | Changes in quality of sleep |
| End point description: | |
| data still being analyzed | |
| End point type | Secondary |
| End point timeframe: | |
| Changes before and after three months of treatment | |

| End point values | Melatonin | Placebo | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: percent | | | | |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Period of reporting: june 2021- february 2022

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

Dictionary used

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

| | |
|--------------------|---|
| Dictionary version | x |
|--------------------|---|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Melatonin |
|-----------------------|-----------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events | Melatonin | Placebo | |
|---|--|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 20 (5.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Transient Cerebral ischaemia | Additional description: Hospitalized. Suspected of TCI. Previous history with TCIs | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 20 (5.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Broken arm | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 0 / 20 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Melatonin | Placebo | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 2 / 20 (10.00%) | |
| General disorders and administration site conditions | | | |

| | | | |
|--|--|--|--|
| Headache subjects affected / exposed occurrences (all) | 1 / 21 (4.76%) 1 | 1 / 20 (5.00%) 1 | |
| Gastrointestinal disorders diarrhea subjects affected / exposed occurrences (all) | 2 / 21 (9.52%) 2 | 0 / 20 (0.00%) 0 | |
| Infections and infestations sore throat subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all) | 0 / 21 (0.00%) 0 1 / 21 (4.76%) 1 | 1 / 20 (5.00%) 1 0 / 20 (0.00%) 0 | |

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