



Clinical trial results:

Prospective, randomised, double-blind, placebo-controlled, single centre phase IIa clinical trial to investigate the safety and tolerability as well as the impact of a substitution of sexual hormones with an estrogen-progestin combination over 10 weeks in addition to in-house psychotherapy on neuro-endocrinological parameters, psychopathology and neuro-psychological performance compared to in-house psychotherapy alone in adult females with anorexia nervosa

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2015-004184-36 |
| Trial protocol | DE |
| Global end of trial date | 14 January 2019 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 12 August 2020 |
| First version publication date | 12 August 2020 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | UKER-AN-HS-01 |
|-----------------------|---------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Universitätsklinikum Erlangen |
| Sponsor organisation address | Schwabachanlage 6, Erlangen, Germany, 91054 |
| Public contact | Psychosomatische Abteilung, Universitätsklinikum Erlangen, +49 91318534898, George.Paslakis@uhn.ca |
| Scientific contact | Psychosomatische Abteilung, Universitätsklinikum Erlangen, George.Paslakis@uhn.ca |

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 | 14 January 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 January 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 January 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Quantification of the impact of the substitution of sexual hormones with an estrogen-progestin combination in addition to in-house psychotherapy on the neuro-psychological performance of female subjects with anorexia nervosa, measured by TMT A and B, Go/NoGo test and WCST

Protection of trial subjects:

Each subject was examined by a gynecologist prior to randomization and was excluded from study participation in case of contraindications (smoker, vascular complications in medical history or family history). Inpatient Setting during the entire period of participation with regular physical examinations, lab checks etc.

Background therapy:

Inpatient psychotherapy

Evidence for comparator:

Placebo-controlled

| | |
|---|-----------------|
| Actual start date of recruitment | 04 January 2016 |
| 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 | Germany: 11 |
| Worldwide total number of subjects | 11 |
| EEA total number of subjects | 11 |

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) | 11 |

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

females aged between 18 and 45 years, Anorexia nervosa acc. DSM 5 or sub-syndromal Anorexia nervosa, BMI ≥ 13 kg/m² and $\leq 18,5$ kg/m²

Period 1

| | |
|------------------------------|---|
| Period 1 title | Screening |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Assessor |

Arms

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

Arm description: -

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | MAXIM 0,030mg/2mg coated tablet, encapsulated |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

daily dose: 1 capsule (0,03mg ethinylestradiol / 2mg dienogest), Duration of Administration: 10 weeks

| | |
|------------------|---------|
| Arm title | Control |
|------------------|---------|

Arm description: -

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

Dosage and administration details:

Daily dose: 1 capsule; Duration of Administration: 10 weeks

| Number of subjects in period 1 | Verum | Control |
|--------------------------------|-------|---------|
| Started | 6 | 5 |
| Completed | 6 | 5 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | Treatment |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Assessor |

Arms

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

Arm description: -

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | MAXIM 0,030mg/2mg coated tablet, encapsulated |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

daily dose: 1 capsule (0,03mg ethinylestradiol / 2mg dienogest), Duration of Administration: 10 weeks

| | |
|------------------|---------|
| Arm title | Control |
|------------------|---------|

Arm description: -

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

Dosage and administration details:

Daily dose: 1 capsule; Duration of Administration: 10 weeks

| Number of subjects in period 2 | Verum | Control |
|---------------------------------------|-------|---------|
| Started | 6 | 5 |
| Completed | 4 | 5 |
| Not completed | 2 | 0 |
| Consent withdrawn by subject | 1 | - |
| Adverse event, non-fatal | 1 | - |

Period 3

| | |
|------------------------------|---|
| Period 3 title | Post-treatment |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Assessor |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|-------|
| Arm title | Verum |
|------------------|-------|

Arm description: -

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | MAXIM 0,030mg/2mg coated tablet, encapsulated |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

daily dose: 1 capsule (0,03mg ethinylestradiol / 2mg dienogest), Duration of Administration: 10 weeks

| | |
|------------------|---------|
| Arm title | Control |
|------------------|---------|

Arm description: -

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

Dosage and administration details:

Daily dose: 1 capsule; Duration of Administration: 10 weeks

| Number of subjects in period 3 | Verum | Control |
|---------------------------------------|-------|---------|
| Started | 4 | 5 |
| Completed | 4 | 3 |
| Not completed | 0 | 2 |
| Lost to follow-up | - | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Screening |
|-----------------------|-----------|

Reporting group description: -

| Reporting group values | Screening | Total | |
|---|-----------|-------|--|
| Number of subjects | 11 | 11 | |
| 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 | | | |
| arithmetic mean | 25.27 | | |
| standard deviation | ± 7.90 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 11 | 11 | |
| Male | 0 | 0 | |
| BMI | | | |
| Units: kg per square meter | | | |
| arithmetic mean | 15.75 | | |
| standard deviation | ± 1.59 | - | |
| TMT A | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | |
| standard deviation | ± | - | |
| TMT B | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | |
| standard deviation | ± | - | |
| WCST errors | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | |
| standard deviation | ± | - | |
| WCST perseveration | | | |

| | | | |
|--|--|-------|---|
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| EDE-Q | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| EDI-2 | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| STAI state | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| STAI trait | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| STAI trait | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| go/no-go test: Reaction times (RT) | | | |
| evaluated at V3 (day1): Food-shift: Verum: 398.89 +/- 31.58; Placebo: 379.29 +/- 23.87 Food-nonshift: Verum: 384.31 +/- 29.96; Placebo: 379.94 +/- 24.57 Neutral-shift: Verum: 403.54 +/- 25.66; Placebo: 385.40 +/- 17.97 Neutral-nonshift: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| go/no-go test: Commission errors (CE) | | | |
| evaluated at V3 (day1): Food-shift: Verum: 3.75 +/- 3.20; Placebo: 4.80 +/- 6.42 Food-nonshift: Verum: 1.00 +/- 1.16; Placebo: 2.80 +/- 2.78 Neutral-shift: Verum: 6.25 +/- 4.50; Placebo: 7.80 +/- 1.64 Neutral-nonshift: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| PHQ-9 | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| EDQoL | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | | \pm | - |
| LH Units: Unit(s)/litre | | | |

| | | | |
|---|-------|---|--|
| arithmetic mean standard deviation | \pm | - | |
| FSH Units: Unit(s)/litre arithmetic mean standard deviation | \pm | - | |
| Estradiol Units: nanogram(s)/litre arithmetic mean standard deviation | \pm | - | |
| Testosterone Units: microgram(s)/litre arithmetic mean standard deviation | \pm | - | |
| Cortisol Units: unit(s) arithmetic mean standard deviation | \pm | - | |
| Ghrelin-OGTT | | | |
| 0 min: Verum: 537.41 +/- 122.43; Placebo: 963.26 +/- 266.79 30 min: Verum: 417.64 +/- 129.85; Placebo: 814.96 +/- 175.24 60 min: Verum: 399.14 +/- 108.48; Placebo: 749.55 +/- 218.63 90 min: Verum: 413.94 +/- 123.93; Placebo: 700.69 +/- 210.80 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | - | |
| Leptin-OGTT | | | |
| 0 min: Verum: 9.33 +/- 6.01; Placebo: 1.26 +/- 1.60 30 min: Verum: 9.07 +/- 4.95; Placebo: 0.82 +/- 0.89 60 min: Verum: 9.37 +/- 5.10; Placebo: 1.04 +/- 1.28 90 min: Verum: 7.79 +/- 4.58; Placebo: 0.94 +/- 1.16 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | - | |
| Insulin-OGTT | | | |
| 0 min: Verum: 10.60 +/- 2.96; Placebo: 4.40 +/- 2.52 30 min: Verum: 78.08 +/- 18.28; Placebo: 64.37 +/- 40.40 60 min: Verum: 83.10 +/- 37.71; Placebo: 74.04 +/- 56.71 90 min: Verum: 70.48 +/- 47.50; Placebo: 77.30 +/- 49.68 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | - | |
| Glucose-OGTT | | | |
| 0 min: Verum: 95.95 +/- 15.77; Placebo: 85.73 +/- 8.81 30 min: Verum: 156.87 +/- 44.23; Placebo: 134.08 +/- 27.36 60 min: Verum: 129.90 +/- 56.59; Placebo: 146.46 +/- 55.91 90 min: Verum: 104.80 +/- 36.75; Placebo: 136.00 +/- 61.13 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | - | |

Subject analysis sets

| | |
|--|--------------------|
| Subject analysis set title | Verum Group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to Verum and treated for 10 weeks (until v6) | |
| Subject analysis set title | Placebo group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to Placebo and treated for 10 weeks (until v6) | |
| Subject analysis set title | Verum group II |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to Verum, treated for 10 weeks (until v6) and followed up until v7 (day 113 +/- 7 days) | |
| Subject analysis set title | Placebo Group II |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to placebo, treated for 10 weeks (until v6) and followed up until v7 (day 113 +/- 7 days) | |

| Reporting group values | Verum Group | Placebo group | Verum group II |
|---|------------------|-----------------|----------------|
| Number of subjects | 4 | 5 | 4 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean standard deviation | ± | ± | ± |
| Gender categorical Units: Subjects | | | |
| Female Male | | | |
| BMI Units: kg per square meter | | | |
| arithmetic mean standard deviation | 16.38 ± 1.73 | 15.22 ± 1.75 | ± |
| TMT A | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean standard deviation | 29.50 ± 10.78 | 28.37 ± 7.76 | ± |

| | | | |
|--|---------|---------|---------|
| TMT B | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | 41.52 | 53.45 | |
| standard deviation | ± 6.81 | ± 24.61 | ± |
| WCST errors | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | 11.25 | 7.60 | |
| standard deviation | ± 10.05 | ± 2.30 | ± |
| WCST perseveration | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | 5.00 | 4.00 | |
| standard deviation | ± 4.08 | ± 0.71 | ± |
| EDE-Q | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | 3.18 |
| standard deviation | ± | ± | ± 1.28 |
| EDI-2 | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | 312.25 |
| standard deviation | ± | ± | ± 85.11 |
| STAI state | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | 52.50 |
| standard deviation | ± | ± | ± 15.20 |
| STAI trait | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | 58.50 |
| standard deviation | ± | ± | ± 14.64 |
| go/no-go test: Reaction times (RT) | | | |
| evaluated at V3 (day1): Food-shift: Verum: 398.89 +/- 31.58; Placebo: 379.29 +/- 23.87 Food-nonshift: Verum: 384.31 +/- 29.96; Placebo: 379.94 +/- 24.57 Neutral-shift: Verum: 403.54 +/- 25.66; Placebo: 385.40 +/- 17.97 Neutral-nonshift: see below | | | |
| Units: unit(s) | | | |
| arithmetic mean | 400.20 | 396.00 | |
| standard deviation | ± 23.54 | ± 29.84 | ± |
| go/no-go test: Commission errors (CE) | | | |
| evaluated at V3 (day1): Food-shift: Verum: 3.75 +/- 3.20; Placebo: 4.80 +/- 6.42 Food-nonshift: Verum: 1.00 +/- 1.16; Placebo: 2.80 +/- 2.78 Neutral-shift: Verum: 6.25 +/- 4.50; Placebo: 7.80 +/- 1.64 Neutral-nonshift: see below | | | |
| Units: unit(s) | | | |
| arithmetic mean | 4.00 | 5.20 | |
| standard deviation | ± 3.65 | ± 3.03 | ± |
| PHQ-9 | | | |

| | | | |
|---|----------|----------|---------|
| evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | 0.75 |
| standard deviation | ± | ± | ± 0.50 |
| EDQoL | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | 34.75 |
| standard deviation | ± | ± | ± 19.38 |
| LH | | | |
| Units: Unit(s)/litre | | | |
| arithmetic mean | 2.55 | 3.87 | |
| standard deviation | ± 2.16 | ± 3.94 | ± |
| FSH | | | |
| Units: Unit(s)/litre | | | |
| arithmetic mean | 3.14 | 4.32 | |
| standard deviation | ± 1.43 | ± 3.44 | ± |
| Estradiol | | | |
| Units: nanogram(s)/litre | | | |
| arithmetic mean | 50.70 | 16.49 | |
| standard deviation | ± 87.81 | ± 28.56 | ± |
| Testosterone | | | |
| Units: microgram(s)/litre | | | |
| arithmetic mean | 0.13 | 0.13 | |
| standard deviation | ± 0.08 | ± 0.04 | ± |
| Cortisol | | | |
| Units: unit(s) | | | |
| arithmetic mean | 8.62 | 73.04 | |
| standard deviation | ± 1.84 | ± 81.44 | ± |
| Ghrelin-OGTT | | | |
| 0 min: Verum: 537.41 +/- 122.43; Placebo: 963.26 +/- 266.79 30 min: Verum: 417.64 +/- 129.85; Placebo: 814.96 +/- 175.24 60 min: Verum: 399.14 +/- 108.48; Placebo: 749.55 +/- 218.63 90 min: Verum: 413.94 +/- 123.93; Placebo: 700.69 +/- 210.80 120 min: see below | | | |
| Units: unit(s) | | | |
| arithmetic mean | 403.73 | 734.98 | |
| standard deviation | ± 157.86 | ± 248.21 | ± |
| Leptin-OGTT | | | |
| 0 min: Verum: 9.33 +/- 6.01; Placebo: 1.26 +/- 1.60 30 min: Verum: 9.07 +/- 4.95; Placebo: 0.82 +/- 0.89 60 min: Verum: 9.37 +/- 5.10; Placebo: 1.04 +/- 1.28 90 min: Verum: 7.79 +/- 4.58; Placebo: 0.94 +/- 1.16 120 min: see below | | | |
| Units: unit(s) | | | |
| arithmetic mean | 8.69 | 1.05 | |
| standard deviation | ± 5.06 | ± 1.33 | ± |
| Insulin-OGTT | | | |
| 0 min: Verum: 10.60 +/- 2.96; Placebo: 4.40 +/- 2.52 30 min: Verum: 78.08 +/- 18.28; Placebo: 64.37 +/- 40.40 60 min: Verum: 83.10 +/- 37.71; Placebo: 74.04 +/- 56.71 90 min: Verum: 70.48 +/- 47.50; Placebo: 77.30 +/- 49.68 120 min: see below | | | |
| Units: unit(s) | | | |
| arithmetic mean | 75.09 | 105.31 | |

| | | | |
|--|---------|----------|---|
| standard deviation | ± 46.45 | ± 109.48 | ± |
| Glucose-OGTT | | | |
| 0 min: Verum: 95.95 +/- 15.77; Placebo: 85.73 +/- 8.81 30 min: Verum: 156.87 +/- 44.23; Placebo: 134.08 +/- 27.36 60 min: Verum: 129.90 +/- 56.59; Placebo: 146.46 +/- 55.91 90 min: Verum: 104.80 +/- 36.75; Placebo: 136.00 +/- 61.13 120 min: see below | | | |
| Units: unit(s) | | | |
| arithmetic mean | 97.74 | 106.21 | |
| standard deviation | ± 6.74 | ± 42.85 | ± |

| | | | |
|---|------------------|--|--|
| Reporting group values | Placebo Group II | | |
| Number of subjects | 3 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |
| BMI | | | |
| Units: kg per square meter | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| TMT A | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| TMT B | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| WCST errors | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |

| | | | |
|--|-----------------------|--|--|
| WCST perseveration | | | |
| neuropsychological Performance test, evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | | |
| EDE-Q | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | 3.57 \pm 0.57 | | |
| EDI-2 | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | 324.33 \pm 69.90 | | |
| STAI state | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | 45.67 \pm 17.62 | | |
| STAI trait | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | 54.67 \pm 13.58 | | |
| go/no-go test: Reaction times (RT) | | | |
| evaluated at V3 (day1): Food-shift: Verum: 398.89 +/- 31.58; Placebo: 379.29 +/- 23.87 Food-nonshift: Verum: 384.31 +/- 29.96; Placebo: 379.94 +/- 24.57 Neutral-shift: Verum: 403.54 +/- 25.66; Placebo: 385.40 +/- 17.97 Neutral-nonshift: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | | |
| go/no-go test: Commission errors (CE) | | | |
| evaluated at V3 (day1): Food-shift: Verum: 3.75 +/- 3.20; Placebo: 4.80 +/- 6.42 Food-nonshift: Verum: 1.00 +/- 1.16; Placebo: 2.80 +/- 2.78 Neutral-shift: Verum: 6.25 +/- 4.50; Placebo: 7.80 +/- 1.64 Neutral-nonshift: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | | |
| PHQ-9 | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | 0.67 \pm 0.58 | | |
| EDQoL | | | |
| evaluated at V3 (day1) | | | |
| Units: unit(s) arithmetic mean standard deviation | 35.33 \pm 11.02 | | |
| LH | | | |

| | | | |
|---|-------|--|--|
| Units: Unit(s)/litre arithmetic mean standard deviation | \pm | | |
| FSH Units: Unit(s)/litre arithmetic mean standard deviation | \pm | | |
| Estradiol Units: nanogram(s)/litre arithmetic mean standard deviation | \pm | | |
| Testosterone Units: microgram(s)/litre arithmetic mean standard deviation | \pm | | |
| Cortisol Units: unit(s) arithmetic mean standard deviation | \pm | | |
| Ghrelin-OGTT | | | |
| 0 min: Verum: 537.41 +/- 122.43; Placebo: 963.26 +/- 266.79 30 min: Verum: 417.64 +/- 129.85; Placebo: 814.96 +/- 175.24 60 min: Verum: 399.14 +/- 108.48; Placebo: 749.55 +/- 218.63 90 min: Verum: 413.94 +/- 123.93; Placebo: 700.69 +/- 210.80 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | | |
| Leptin-OGTT | | | |
| 0 min: Verum: 9.33 +/- 6.01; Placebo: 1.26 +/- 1.60 30 min: Verum: 9.07 +/- 4.95; Placebo: 0.82 +/- 0.89 60 min: Verum: 9.37 +/- 5.10; Placebo: 1.04 +/- 1.28 90 min: Verum: 7.79 +/- 4.58; Placebo: 0.94 +/- 1.16 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | | |
| Insulin-OGTT | | | |
| 0 min: Verum: 10.60 +/- 2.96; Placebo: 4.40 +/- 2.52 30 min: Verum: 78.08 +/- 18.28; Placebo: 64.37 +/- 40.40 60 min: Verum: 83.10 +/- 37.71; Placebo: 74.04 +/- 56.71 90 min: Verum: 70.48 +/- 47.50; Placebo: 77.30 +/- 49.68 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | | |
| Glucose-OGTT | | | |
| 0 min: Verum: 95.95 +/- 15.77; Placebo: 85.73 +/- 8.81 30 min: Verum: 156.87 +/- 44.23; Placebo: 134.08 +/- 27.36 60 min: Verum: 129.90 +/- 56.59; Placebo: 146.46 +/- 55.91 90 min: Verum: 104.80 +/- 36.75; Placebo: 136.00 +/- 61.13 120 min: see below | | | |
| Units: unit(s) arithmetic mean standard deviation | \pm | | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Verum |
| Reporting group description: - | |
| Reporting group title | Control |
| Reporting group description: - | |
| Reporting group title | Verum |
| Reporting group description: - | |
| Reporting group title | Control |
| Reporting group description: - | |
| Reporting group title | Verum |
| Reporting group description: - | |
| Reporting group title | Control |
| Reporting group description: - | |
| Subject analysis set title | Verum Group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to Verum and treated for 10 weeks (until v6) | |
| Subject analysis set title | Placebo group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to Placebo and treated for 10 weeks (until v6) | |
| Subject analysis set title | Verum group II |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to Verum, treated for 10 weeks (until v6) and followed up until v7 (day 113 +/- 7 days) | |
| Subject analysis set title | Placebo Group II |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: subjects randomized to placebo, treated for 10 weeks (until v6) and followed up until v7 (day 113 +/- 7 days) | |

Primary: Change of the neuropsychological performance measured by TMT A after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone

| | |
|---|--|
| End point title | Change of the neuropsychological performance measured by TMT A after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone |
| End point description: | |
| End point type | Primary |
| End point timeframe: visit 6 (day 73 +/- 3 days) | |

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 27.27 (± 5.59) | 26.63 (± 8.40) | | |

Statistical analyses

| Statistical analysis title | TMT A |
|---|-----------------------------|
| Statistical analysis description: Change in TMT A between V3 and V6 compared between Verum Group and Placebo group | |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 9 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.86 ^[1] |
| Method | ANOVA |

Notes:

[1] - rm-ANOVA with 1rm factor (pre:V3/post:V6); TMT A as dependent variable and Group (Placebo vs. Verum) as between-subject factor.

Primary: Change of the neuropsychological performance measured by TMT B after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone

| | |
|-----------------|--|
| End point title | Change of the neuropsychological performance measured by TMT B after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone |
|-----------------|--|

End point description:

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: visit 6 (day 73 +/- 3 days) | |

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 39.28 (± 3.71) | 35.50 (± 3.51) | | |

Statistical analyses

| Statistical analysis title | TMT B |
|----------------------------|-------|
|----------------------------|-------|

Statistical analysis description:

Change in TMT B between v3 (day 1) and v6 (day 73+/-3) compared between Verum Group and Placebo

| | |
|---|-----------------------------|
| Group | |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 9 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6 ^[2] |
| Method | ANOVA |

Notes:

[2] - rm ANOVA with 1rm factor (pre/post), TMT B as dependent variable and Group (Placebo vs. Verum) as between-subject factor.

Primary: Change of the neuropsychological performance measured by WCST errors after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) in the intervention group vs. the group with psychotherapy alone

| | |
|-----------------|---|
| End point title | Change of the neuropsychological performance measured by WCST errors after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) in the intervention group vs. the group with psychotherapy alone |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 7.50 (± 1.29) | 6.80 (± 1.64) | | |

Statistical analyses

| | |
|-----------------------------------|-------------|
| Statistical analysis title | WCST errors |
|-----------------------------------|-------------|

Statistical analysis description:

Change in WCST Errors between visit 3 (day1) and visit 6 (day 73+/-3) compared between Verum Group and Placebo group

| | |
|---|-----------------------------|
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 9 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.42 ^[3] |
| Method | ANOVA |

Notes:

[3] - rm-ANOVA with 1 factor (pre/post), WCST Errors as dependent variable and Group as between-subject factor.

Primary: Change of the neuropsychological performance measured by WCST perseveration after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) in the intervention group vs. the group with psychotherapy

alone

| | |
|-----------------|--|
| End point title | Change of the neuropsychological performance measured by WCST perseveration after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) in the intervention group vs. the group with psychotherapy alone |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 3.75 (\pm 0.50) | 2.80 (\pm 1.30) | | |

Statistical analyses

| | |
|-----------------------------------|--------------------|
| Statistical analysis title | WCST perseveration |
|-----------------------------------|--------------------|

Statistical analysis description:

Change in WCST Perseveration between visit 3 (day 1) and visit 6 (day 73 +/- 3 days) compared between Verum Group and Placebo group

| | |
|---|-----------------------------|
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 9 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.37 ^[4] |
| Method | ANOVA |

Notes:

[4] - rm ANOVA with 1 factor (pre/post), WCST Perseveration as dependent variable and Group as between-subject factor

Primary: Change of the neuropsychological performance measured by go/no-go test: RT after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone

| | |
|-----------------|--|
| End point title | Change of the neuropsychological performance measured by go/no-go test: RT after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone |
|-----------------|--|

End point description:

Food-shift: Verum: 387.99 +/- 22.19; Placebo: 372.58 +/- 20.90

Food-nonshift: Verum: 385.39 +/- 30.98; Placebo: 370.72 +/- 19.68

Neutral-shift: Verum: 382.99 +/- 20.15; Placebo: 390.28 +/- 18.18

Neutral-nonshift: see below

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 384.12 (\pm 15.12) | 378.63 (\pm 20.30) | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | go/no-go: Reaction times (RT) |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 9 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.54 ^[5] |
| Method | ANOVA |

Notes:

[5] - rm ANOVA with 3 rm factors (category: Food vs. neutral; shift-Status: shift vs. non-shift; time: V3/V6/V7); significant main effect of time ($p=0.013$); significant main effect of category ($p=0.036$); no main effect for group

Primary: Change of the neuropsychological performance measured by go/no-go test: CE after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone

| | |
|-----------------|--|
| End point title | Change of the neuropsychological performance measured by go/no-go test: CE after 10 weeks of psychotherapy and sexual hormone substitution compared to V3 (day1) the intervention group vs. the group with psychotherapy alone |
|-----------------|--|

End point description:

Food-shift: Verum: 3.25 \pm 2.22; Placebo: 2.60 \pm 2.30
Food-nonshift: Verum: 1.25 \pm 1.26; Placebo: 2.8 \pm 1.64
Neutral-shift: Verum: 3.75 \pm 1.89; Placebo: 7.60 \pm 2.07
Neutral-nonshift: see below

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

visit 7 (day 113 \pm 7 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 3.75 (\pm 1.89) | 3.80 (\pm 1.64) | | |

Statistical analyses

| | |
|---|---------------------------------------|
| Statistical analysis title | go/no-go test: Commission errors (CE) |
| Comparison groups | Placebo group v Verum Group |
| Number of subjects included in analysis | 9 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.38 ^[6] |
| Method | ANOVA |

Notes:

[6] - rm ANOVA with 3 rm factors (category: Food vs. neutral; shift-Status: shift vs. non-shift; time: V3/V6/V7); significant main effect for shift Status ($p < 0.001$); significant main effect for category ($p = 0.005$); no main effect for time ($p = 0.15$) or group

Secondary: change in scores of subscales "eating concern", "weight concern" and "shape concern" measured by the EDE-Q

| | |
|-----------------|--|
| End point title | change in scores of subscales "eating concern", "weight concern" and "shape concern" measured by the EDE-Q |
|-----------------|--|

End point description:

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

End point timeframe:

visit 7 (day 113 +/- 7 days)

| | | | | |
|--------------------------------------|----------------------|----------------------|--|--|
| End point values | Verum group II | Placebo Group II | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 2.06 (\pm 1.38) | 1.44 (\pm 1.11) | | |

Statistical analyses

| | |
|--|-----------------------------------|
| Statistical analysis title | EDE-Q |
| Statistical analysis description: | |
| Change in EDE-Q between V3, V6 and V7 compared between Verum Group and Placebo group | |
| Comparison groups | Verum group II v Placebo Group II |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.87 ^[7] |
| Method | ANOVA |

Notes:

[7] - rm-ANOVA with 1 rm factor (V3/V6/V7), EDE-Q as dependent variable and Group as between-subject factor

Secondary: change in psychopathology measured by EDI-2

| | |
|-----------------|---|
| End point title | change in psychopathology measured by EDI-2 |
|-----------------|---|

End point description:

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

End point timeframe:

visit 7 (day 113 +/- 7 days)

| End point values | Verum group II | Placebo Group II | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 277.00 (± 64.08) | 263.67 (± 115.24) | | |

Statistical analyses

| | |
|----------------------------|-------|
| Statistical analysis title | EDI-2 |
|----------------------------|-------|

Statistical analysis description:

Change in EDI-2 between V3, V6 and V7 compared between Verum Group and Placebo group

| | |
|---|-----------------------------------|
| Comparison groups | Verum group II v Placebo Group II |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.93 ^[8] |
| Method | ANOVA |

Notes:

[8] - rm-ANOVA with 1 rm factor (V3/V6/V7), EDE-Q as dependent variable and Group as between-subject factor.

Secondary: change in state anxiety measured by STAI state

| | |
|-----------------|--|
| End point title | change in state anxiety measured by STAI state |
|-----------------|--|

End point description:

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

End point timeframe:

visit 7 (day 113 +/- 7 days)

| End point values | Verum group II | Placebo Group II | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 48.00 (\pm 13.37) | 44.67 (\pm 16.62) | | |

Statistical analyses

| Statistical analysis title | STAI state |
|--|-----------------------------------|
| Statistical analysis description: Change in STAI state between V3, V6 and V7 compared between Verum Group and Placebo group | |
| Comparison groups | Verum group II v Placebo Group II |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.58 [9] |
| Method | ANOVA |

Notes:

[9] - rm ANOVA with 1 rm factor (V3/V6/V7), STAI state as Independent variable and Group as between-subject factor.

Secondary: change in depressive co-morbidity measured by PHQ-9

| | |
|--|---|
| End point title | change in depressive co-morbidity measured by PHQ-9 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: visit 7 (day 113 +/- 7 days) | |

| End point values | Verum group II | Placebo Group II | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 0.25 (\pm 0.50) | 0.33 (\pm 0.58) | | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | PHQ-9 |
| Comparison groups | Verum group II v Placebo Group II |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.88 ^[10] |
| Method | ANOVA |

Notes:

[10] - rm ANOVA with 1 factor (V3/V6/V7), PHQ-9 as Independent variable and Group as between-subject factor

Secondary: change in quality of life associated with eating disorders measured by EDQoL

| | |
|-----------------|--|
| End point title | change in quality of life associated with eating disorders measured by EDQoL |
|-----------------|--|

End point description:

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

End point timeframe:

visit 7 (day 113 +/- 7 days)

| | | | | |
|--------------------------------------|----------------------|----------------------|--|--|
| End point values | Verum group II | Placebo Group II | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 23.25 (± 18.25) | 14.00 (± 11.27) | | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | EDQoL |
| Comparison groups | Verum group II v Placebo Group II |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.84 ^[11] |
| Method | ANOVA |

Notes:

[11] - rm ANOVA with 1 rm factor (V3/V6/V7), EDQoL as Independent variable and group as between-subject factor

Secondary: change of plasma cortisol levels during a dexamethason suppression test

| | |
|-----------------|---|
| End point title | change of plasma cortisol levels during a dexamethason suppression test |
|-----------------|---|

End point description:

| | |
|-----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| visit 6 (day 73 +/- 3 days) | |

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[12] | 4 ^[13] | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 36.92 (± 9.64) | 70.66 (± 85.54) | | |

Notes:

[12] - in one subject no values available

[13] - in one subject no values available

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | Cortisol |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.36 ^[14] |
| Method | ANOVA |

Notes:

[14] - rm ANOVA with 1 rm factor (time), Cortisol concentrations as dependent variable and Group as between-subject factor.

Secondary: change of sexual hormone plasma levels: LH

| | |
|------------------------|--|
| End point title | change of sexual hormone plasma levels: LH |
| End point description: | |

| | |
|-----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| visit 6 (day 73 +/- 3 days) | |

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[15] | 3 ^[16] | | |
| Units: Unit(s)/litre | | | | |
| arithmetic mean (standard deviation) | 0.11 (± 0.19) | 3.34 (± 2.93) | | |

Notes:

[15] - in one subject no values available

[16] - in two subjects no values available

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | LH |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 6 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.28 ^[17] |
| Method | ANOVA |

Notes:

[17] - rm ANOVA with 1 rm factor (time), LH as dependent variable and Group as between-subject factor

Secondary: change of plasma levels of appetite-regulating peptides: Ghrelin

| | |
|--|--|
| End point title | change of plasma levels of appetite-regulating peptides: Ghrelin |
| End point description: | |
| 0 min: Verum: 432.96 +/- 188.20; Placebo: 762.79 +/- 241.07 | |
| 30 min: Verum: 342.58 +/- 174.46; Placebo: 700.78 +/- 301.00 | |
| 60 min: Verum: 281.27 +/- 148.63; Placebo: 636.42 +/- 255.08 | |
| 90 min: Verum: 291.24 +/- 153.63; Placebo: 642.78 +/- 270.31 | |
| 120 min: see below | |
| End point type | Secondary |
| End point timeframe: | |
| visit 6 (day 73 +/- 3 days) | |

| | | | | |
|--------------------------------------|----------------------|----------------------|--|--|
| End point values | Verum Group | Placebo group | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[18] | 4 ^[19] | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 320.11 (± 138.06) | 691.18 (± 271.94) | | |

Notes:

[18] - in one subject no values available

[19] - in one subject no values available

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | Ghrelin-OGTT |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.07 ^[20] |
| Method | ANOVA |

Notes:

[20] - rm ANOVA with 2 rm factors (OGTT time Points; time pre/post), Ghrelin concentrations as dependent variable and Group as between-subject factor

Secondary: number of AE

| | |
|------------------------|--------------|
| End point title | number of AE |
| End point description: | |
| End point type | Secondary |

End point timeframe:
from visit 3 (day 1) to visit 7 (day 113 +/- 7 days)

| End point values | Verum | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6 | 5 | | |
| Units: whole numbers >/= 0 | 6 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in trait anxiety measured by STAI trait

| | |
|--|--|
| End point title | Change in trait anxiety measured by STAI trait |
| End point description: | |
| End point type | Secondary |
| End point timeframe: visit 7 (day 113 +/- 7 days) | |

| End point values | Verum group II | Placebo Group II | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 48.50 (± 15.16) | 42.67 (± 18.77) | | |

Statistical analyses

| | |
|--|-----------------------------------|
| Statistical analysis title | STAI trait |
| Statistical analysis description: Change in STAI trait between V3, V6 and V7 compared between Verum Group and Placebo group | |
| Comparison groups | Verum group II v Placebo Group II |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.66 ^[21] |
| Method | ANOVA |

Notes:

[21] - rm ANOVA with 1 factor (V3/V6/V7), STAI trait as Independent variable and Group as between-subject factor.

Secondary: change of sexual hormone plasma levels: FSH

| | |
|-----------------|---|
| End point title | change of sexual hormone plasma levels: FSH |
|-----------------|---|

End point description:

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

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[22] | 3 ^[23] | | |
| Units: Unit(s)/litre | | | | |
| arithmetic mean (standard deviation) | 0.17 (± 0.29) | 3.48 (± 2.63) | | |

Notes:

[22] - In one subject value missing

[23] - In two subjects value missing

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | FSH |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 6 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.14 ^[24] |
| Method | ANOVA |

Notes:

[24] - rm ANOVA with 1 rm factor (time), FSH as dependent variable and Group as between-subject factor.

Secondary: change of sexual hormone plasma levels: Estradiol

| | |
|-----------------|---|
| End point title | change of sexual hormone plasma levels: Estradiol |
|-----------------|---|

End point description:

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

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[25] | 3 ^[26] | | |
| Units: nanogram(s)/litre | | | | |
| arithmetic mean (standard deviation) | 0 (± 0) | 42.25 (± 55.05) | | |

Notes:

[25] - in one subject no value available

[26] - in two subjects no value available

Statistical analyses

| Statistical analysis title | Estradiol |
|---|-----------------------------|
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 6 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.53 ^[27] |
| Method | ANOVA |

Notes:

[27] - rm ANOVA with 1 rm factor (time), estradiol as dependent variable and Group as between-subject factor.

Secondary: change of sexual hormone plasma levels: Testosteron

| | |
|-----------------|---|
| End point title | change of sexual hormone plasma levels: Testosteron |
|-----------------|---|

End point description:

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

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[28] | 3 ^[29] | | |
| Units: microgram(s)/litre | | | | |
| arithmetic mean (standard deviation) | 0.16 (± 0.07) | 0.13 (± 0.05) | | |

Notes:

[28] - in one subject no value available

[29] - in two subjects no value available

Statistical analyses

| Statistical analysis title | Testosteron |
|----------------------------|-----------------------------|
| Comparison groups | Verum Group v Placebo group |

| | |
|---|------------------------|
| Number of subjects included in analysis | 6 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.28 ^[30] |
| Method | ANOVA |

Notes:

[30] - rm ANOVA with 1 rm factor (time), Testosterone as dependent variable and Group as between-subject factor

Secondary: change of plasma levels of appetite-regulating peptides: Leptin

| | |
|-----------------|---|
| End point title | change of plasma levels of appetite-regulating peptides: Leptin |
|-----------------|---|

End point description:

0 min: Verum: 21.84 +/- 11.15; Placebo: 3.33 +/- 2.72

30 min: Verum: 18.99 +/- 5.38; Placebo: 2.99 +/- 2.34

60 min: Verum: 15.49 +/- 6.38; Placebo: 3.08 +/- 2.68

90 min: Verum: 18.60 +/- 7.84; Placebo: 2.95 +/- 2.50

120 min: see below

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

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[31] | 4 ^[32] | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 19.13 (± 9.61) | 3.45 (± 3.27) | | |

Notes:

[31] - in one subject no values available

[32] - in one subject no values available

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | Leptin-OGTT |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.016 ^[33] |
| Method | ANOVA |

Notes:

[33] - rm ANOVA with 2 rm factors (OGTT time Points and pre/post), Leptin concentrations as dependent variable and Group as between-subject factor

Secondary: change of plasma levels of Insulin

| | |
|-----------------|------------------------------------|
| End point title | change of plasma levels of Insulin |
|-----------------|------------------------------------|

End point description:

0 min: Verum: 11.39 +/- 4.67; Placebo: 6.45 +/- 3.57

30 min: Verum: 79.66 +/- 45.12; Placebo: 48.38 +/- 21.61

60 min: Verum: 88.00 +/- 33.64; Placebo: 42.91 +/- 19.23

90 min: Verum: 91.46 +/- 55.16; Placebo: 44.73 +/- 25.84

120 min: see below

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

End point timeframe:
visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[34] | 4 ^[35] | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 79.56 (± 26.29) | 21.91 (± 12.69) | | |

Notes:

[34] - in one subject no values available

[35] - in one subject no values available

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | Insulin-OGTT |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.44 ^[36] |
| Method | ANOVA |

Notes:

[36] - rm ANOVA with 2 rm factors (time Point of the OGTT and pre/post), Insulin concentrations as the dependent variable and Group as between-subject factor.

Secondary: change of plasma levels of Glucose

| | |
|---|------------------------------------|
| End point title | change of plasma levels of Glucose |
| End point description: 0 min: Verum: 107.19 +/- 21.59; Placebo: 84.37 +/- 11.28 30 min: Verum: 178.20 +/- 64.42; Placebo: 125.20 +/- 25.07 60 min: Verum: 152.73 +/- 46.07; Placebo: 107.54 +/- 55.02 90 min: Verum: 131.09 +/- 29.29; Placebo: 90.04 +/- 32.33 120 min: see below | |
| End point type | Secondary |

End point timeframe:

visit 6 (day 73 +/- 3 days)

| End point values | Verum Group | Placebo group | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3 ^[37] | 4 ^[38] | | |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | 122.36 (± 31.26) | 77.64 (± 16.96) | | |

Notes:

[37] - in one subject no values available

[38] - in one subject no values available

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | Glucose-OGTT |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 7 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.44 ^[39] |
| Method | ANOVA |

Notes:

[39] - rm ANOVA with 2 rm factors (OGTT time Points and pre/post), Glucose concentration as dependent variable and Group as between-subject factor.

Other pre-specified: Change in BMI

| | |
|-----------------|---------------|
| End point title | Change in BMI |
|-----------------|---------------|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

visit 6 (day 73 +/- 3 days)

| | | | | |
|--------------------------------------|----------------------|----------------------|--|--|
| End point values | Verum Group | Placebo group | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: kg/m ² | | | | |
| arithmetic mean (standard deviation) | 18.45 (± 1.59) | 17.66 (± 1.97) | | |

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | BMI |
| Comparison groups | Verum Group v Placebo group |
| Number of subjects included in analysis | 9 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.49 ^[40] |
| Method | ANOVA |

Notes:

[40] - rm ANOVA with 1 rm factor (time); significant main effect for time (p=0.023), no main effect for group

Adverse events

Adverse events information

Timeframe for reporting adverse events:

visit 3 (day 1) to visit 7 (day 113 +/- 7 days)

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Verum |
|-----------------------|-------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events | Verum | Control | |
|---|----------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (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: 5 %

| Non-serious adverse events | Verum | Control | |
|---|----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 3 / 5 (60.00%) | |
| Investigations | | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood thyroid stimulating hormone increased | | | |

| | | | |
|---|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 5 (0.00%) 0 | |
| Injury, poisoning and procedural complications Concussion subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 5 (0.00%) 0 | |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 5 (20.00%) 1 | |
| General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 1 / 5 (20.00%) 1 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 5 (20.00%) 1 | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 6 (16.67%) 1 | 0 / 5 (0.00%) 0 | |
| Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all) | 0 / 6 (0.00%) 0 | 1 / 5 (20.00%) 2 | |

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

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

| |
|--|
| Early Termination due to poor recruitment, therefore no reliable statistical analyses could be performed |
|--|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29631553>