

GENERAL INFORMATION OF THE CLINICAL TRIAL

| | |
|--------------------------|--|
| RPCEC code | RPCEC00000421 |
| Public title | Dietzia safety study |
| Scientific title | Safety evaluation of Dietzia natronolimnaea C79793-74 for its use as a probiotic in humans". |
| Intervention description | two |

PARTICIPANT FLOW

| | |
|-------------------|-----|
| Evaluated | 120 |
| Excluded | 0 |
| Exclusion cause 1 | n |
| ... | |
| Exclusion cause n | n |
| Randomized | 100 |

| Characteristics | Dietzia Group | Placebo Group | ... | Total |
|---------------------------|------------------|------------------|-----|-------|
| Randomized | 50 | 50 | | 100 |
| Discontinued intervention | 1 | 3 | | 4 |
| Reason 1 | Personal reasons | Personal reasons | | |
| Reason 2 | | | | |
| ... | | | | |
| End of study | 49 | 47 | | 96 |
| Analysis | 49 | 49 | | 98 |

BASELINE CHARACTERISTICS

| Demographic Variables | Dietzia cohort (n=49) | | Placebo (n=49) | | pValue | |
|-----------------------|-----------------------|-------------|----------------|-------------|--------|---------------------|
| | No | % | No | % | | |
| Sex | Female | 36 | 73.5 | 31 | 63.3 | p=0.38 ^a |
| | Male | 13 | 26.5 | 18 | 36.7 | |
| Age | Media±SD | 41.18±17.14 | | 44.43±14.74 | | p=0.29 ^b |
| BMI | Media±SD | 23.57±3.69 | | 23.63±4.17 | | P=0.94 ^b |

OUTCOME MEASURES

a) Primary outcomes

Summary results of Clinical Trial

| Adverse Event | Dietzia (n=49) | | | Placebo (n=49) | | |
|------------------------------------|----------------|----------|--------|----------------|----------|--------|
| | Mild | Moderate | Severe | Mild | Moderate | Severe |
| Abdominal /GI discomfort | 5 (4.1) | 0 | 0 | 0 | 0 | 0 |
| acne rosacea | 0 | 0 | 0 | 0 | 0 | 0 |
| Anxiety Depression | 2(2.0) | 0 | 0 | 0 | 0 | 0 |
| Joint pain | 0 | 0 | 0 | 0 | 0 | 0 |
| Bronchitis | 0 | 0 | 0 | 0 | 0 | 0 |
| Excision of birthmarks | 0 | 0 | 0 | 0 | 0 | 0 |
| Bruises after a fall | 1(1.0) | 0 | 0 | 0 | 0 | 0 |
| Crotid stenosis | 0 | 0 | 0 | 0 | 0 | 0 |
| Cataract Surgery | 0 | 0 | 0 | 0 | 0 | 0 |
| Chondrocalcinosis | 0 | 0 | 0 | 0 | 0 | 0 |
| Colonoscopy and fibroscopy | 0 | 0 | 0 | 0 | 0 | 0 |
| Cystitis | 0 | 0 | 0 | 0 | 0 | 0 |
| Dental pain | 0 | 0 | 0 | 0 | 0 | 0 |
| Diarrhea | 0 | 0 | 0 | 2(2.0) | 0 | 0 |
| Dizziness and nausea | 2(2.0) | 0 | 0 | 0 | 0 | 0 |
| Edema | | 0 | 0 | 0 | 1(1.0) | 0 |
| Gases | 10 (10.2) | 0 | 0 | 0 | 0 | 0 |
| General aches | 0 | 0 | 0 | 0 | 0 | 0 |
| Genital herpes | 0 | 0 | 0 | 0 | 0 | 0 |
| Headache | 2(2.0) | 0 | 0 | 0 | 0 | 0 |
| Hemorrhoids | 0 | 0 | 0 | 0 | 0 | 0 |
| Infection | 0 | 0 | 0 | 0 | 0 | 0 |
| Inflamed prostate | 0 | 0 | 0 | 0 | 0 | 0 |
| Migraine | 0 | 0 | 0 | 0 | 0 | 0 |
| Mouth ulcer | 0 | 0 | 0 | 0 | 0 | 0 |
| Muscle discomfort | 0 | 0 | 0 | 0 | 0 | 0 |
| Nasal obstruction | 0 | 0 | 0 | 0 | 0 | 0 |
| Orthopedic pain | 0 | 0 | 0 | 0 | 0 | 0 |
| Pain following capsule consumption | 4(4.1) | 0 | 0 | 0 | 0 | 0 |
| Palpitations | 0 | 0 | 0 | 0 | 0 | 0 |
| Radio-infiltration (shoulder) | 0 | 0 | 0 | 0 | 0 | 0 |
| Rhinitis | 0 | 0 | 0 | 0 | 0 | 0 |
| Sore throat | 0 | 0 | 0 | 0 | 0 | 0 |

Summary results of Clinical Trial

| | | | | | | |
|--|--------|---|---|---|---|---|
| Tracheitis | 0 | 0 | 0 | 0 | 0 | 0 |
| Trouble sleeping (insomnia) | 2(2.0) | 0 | 0 | 0 | 0 | 0 |
| Vaginal dryness | 0 | 0 | 0 | 0 | 0 | 0 |
| Vagal seizures during or after taking a blood sample. | 0 | 0 | 0 | 0 | 0 | 0 |
| vitamin D deficiency | 0 | 0 | 0 | 0 | 0 | 0 |
| others | 0 | 0 | 0 | 0 | 0 | 0 |

b) Secondary outcomes

| Clinical Chemistry and Hematology | Normal Range | Dietzia Group (n=49) | | Placebo (n=47) | |
|--|--|-------------------------|--------------------|--------------------|--------------------|
| | | Baseline | Day 60 | Baseline | Day 60 |
| Creatinine | 47.6-113.4 μ mol/L | 64,84 \pm 15,5 | 78,63 \pm 18,19 | 73,10 \pm 21,59 | 76,167 \pm 17,84 |
| Urea | <8.3mmol/L | 3,34 \pm 0,99 | 3,96 \pm 1,46 | 4,02 \pm 1,16 | 4,47 \pm 1,12 |
| ALAT | <45U/L | 17,41 \pm 14,20 | 13,77 \pm 4,73 | 19,44 \pm 9,45 | 16,26 \pm 6,71 |
| ASAT | 40U/L | 16,29 \pm 4,93 | 15,02 \pm 5,70 | 18,13 \pm 4,78 | 13,35 \pm 5,01 |
| GGT | <50U/L | 22,78 \pm 33,07 | 19,92 \pm 17,13 | 22,57 \pm 16,62 | 24,80 \pm 20,21 |
| Total Protein | 60-80g/L | 66,02 \pm 3,81 | 69,40 \pm 5,11 | 70,59 \pm 6,22 | 70,77 \pm 4,00 |
| Albumin | 35-52 g/L | 39,83 \pm 4,46 | 43,45 \pm 6,59 | 44,78 \pm 3,38 | 44,65 \pm 2,89 |
| Glycemia | 4.2-6.1 μ mol/L | 4,85 \pm 1,39 | 4,53 \pm 0,49 | 4,74 \pm 0,55 | 4,69 \pm 0,46 |
| Cholesterol | 2.81-5.2 mmol/L | 4,89 \pm 1,09 | 4,15 \pm 1,23 | 4,95 \pm 1,24 | 4,49 \pm 1,11 |
| Triglycerides | 0.46-1.8mmol/L | 1,10 \pm 0,66 | 1,12 \pm 0,69 | 1,29 \pm 0,87 | 1,33 \pm 0,69 |
| Total bilirubin | <17mmol/L | 8,31 \pm 5,33 | 7,14 \pm 4,49 | 9,32 \pm 5,33 | 7,62 \pm 4,49 |
| Direct bilirubin | <5.1mmol/L | 3,20 \pm 1,61 | 3,06 \pm 1,38 | 4,03 \pm 4,59 | 2,95 \pm 1,24 |
| WBC | (4.5-11) x 10 ⁹ / μ L | 6,50 \pm 1,87 | 6,42 \pm 1,75 | 6,26 \pm 1,62 | 6,52 \pm 1,96 |
| RBC | (F=4.2-5.4 / M=4.7-6.1) cels/ μ l | 4,33 \pm 0,41 | 4,43 \pm 0,42 | 4,51 \pm 0,40 | 4,56 \pm 0,39 |
| HBG | (F=12.3-15.3/M=14.0-17.5) g/dL | 127,78 \pm 12,49 | 130,90 \pm 12,19 | 131,53 \pm 15,45 | 132,51 \pm 13,71 |
| HTC | (F=36-45/M=42-50) % | 0,40 \pm 0,03 | 0,41 \pm 0,03 | 0,40 \pm 0,04 | 0,42 \pm 0,03 |
| MVC | 80-96.1% | 93,60 \pm 4,07 | 92,72 \pm 4,35 | 90,79 \pm 6,15 | 92,30 \pm 5,53 |
| MCHC | 33.4-35.5 g/dl | 29,49 \pm 1,37 | 29,39 \pm 1,51 | 29,15 \pm 2,36 | 29,02 \pm 2,13 |
| PLT | (172-450) x10 ³ /mL | 234,39 \pm 52,20 | 236,71 \pm 53,22 | 261,88 \pm 52,73 | 259,67 \pm 62,52 |
| RDWCV | (11-14) % | 13,11 \pm 0,78 | 13,04 \pm 0,86 | 12,82 \pm 1,90 | 13,12 \pm 1,22 |
| MPV | (F: 12-16 / M: 14-17.4) g/dL | 10,16 \pm 0,89 | 10,36 \pm 0,83 | 10,34 \pm 0,90 | 10,35 \pm 0,80 |
| Neutrophil | 1.42-6.34x10 ⁹ /L | 3,87 \pm 1,45 | 3,60 \pm 1,27 | 3,36 \pm 1,16 | 3,66 \pm 1,56 |
| lymphocytes | 0.71-4.53X10 ⁹ /L | 1,94 \pm 0,78 | 2,07 \pm 0,59 | 2,12 \pm 0,63 | 2,10 \pm 0,66 |

Summary results of Clinical Trial

| | | | | | |
|-------------|------------------------------|-------------|-------------|-------------|-------------|
| Monocytes | 0.14-0.72X10 ⁹ /L | 0,54 ± 0,18 | 0,54 ± 0,20 | 0,52 ± 0,13 | 0,52 ± 0,16 |
| eosinophils | 0-0.54X10 ⁹ /L | 0,17 ± 0,16 | 0,16 ± 0,14 | 0,20 ± 0,17 | 0,19 ± 0,13 |
| Basophils | 0-0.18X 10 ⁹ /L | 0,02 ± 0,01 | 0,02 ± 0,01 | 0,02 ± 0,01 | 0,02 ± 0,01 |

| Hemodynamic Parameters | Dietzia Group (n=49) | | Placebo (n=47) | |
|------------------------------------|-------------------------|--------------|-------------------|--------------|
| | Baseline | Day 60 | Baseline | Day 60 |
| Systolic arterial pressure (mmHg) | 119.08±12.40 | 113.55±20.30 | 118.39±12.54 | 115.82±11.41 |
| Diastolic arterial pressure (mmHg) | 74.45±7.86 | 73.27±6.91 | 72.33±9.08 | 71.37±8.96 |
| Heart rate (bpm) | 80.51±11.19 | 80.38±9.88 | 76.43±12.26 | 75.51±12.02 |

ADVERSE EVENTS

| <i>Presence of AE</i> | <i>Dietzia cohort (n=49)</i> | | <i>Placebo (n=49)</i> | | <i>Total No (%)</i> | <i>pValue</i> |
|---------------------------|------------------------------|----------|-----------------------|----------|-------------------------|---------------|
| | <i>No</i> | <i>%</i> | <i>No</i> | <i>%</i> | | |
| <i>No AE</i> | 41 | 83.7 | 46 | 93.9 | 87(88.8) | |
| <i>AE</i> | 8 | 16.2 | 3 | 6.1 | 11 (11.2) | 0.199 |
| <i>Total</i> | 49 | 100 | 49 | 100 | 98 (100) | |