# Clinical trial results:
# Impact of n-3 Polyunsaturated Fatty Acids on Adipose Tissue Inflammation in Morbidly Obese Patients

## Summary

| | |
|---|---|
| EudraCT number | 2006-005287-94 |
| Trial protocol | AT |
| Global end of trial date | 20 February 2012 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 30 July 2020 |
| First version publication date | 30 July 2020 |
| Summary attachment (see zip file) | n-3 PUFA reduce adipose tissue inflammation in obesity (AJCN 2012 BKI.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | Stulnig_PUFA1 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00760760 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Medizinische Universität Wien |
| Sponsor organisation address | Währinger Gürtel 18-20, Wien, Austria, 1090 |
| Public contact | Prof. Thomas M. Stulnig, Medizinische Universität Wien Departement of Medical III, +43 14040043100, thomas.stulnig@meduniwien.ac.at |
| Scientific contact | Prof. Thomas M. Stulnig, Medizinische Universität Wien Departement of Medical III, +43 14040043100, thomas.stulnig@meduniwien.ac.at |

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 | 22 February 2012 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 20 February 2012 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

effect of n-3 polyunsaturated fatty acids (n-3 PUFA; Omacor®) on visceral and subcutaneous adipose tissue inflammation

Protection of trial subjects:

The subjects were allocated to receive either Omacor or Butterfat as control. Both groups tolerated the intervention very well.
During the trial oral glucose tolerance tests were performed without any complications. Adipose tissue samples were collected at the end of the trial during bariatric surgery unter general anesthesia.

Background therapy: -

Evidence for comparator:

n-3 PUFA was supplied in 1 g gelatin capsules containing 90% ethyl esters of n-3 PUFA including 460 mg eicosapentaenoic acid and 380 mg docosahexaenoic
acid as it is available as a drug ("Omacor"®). Four capsules were taken daily, i.e. 3,6 g n-3 PUFA per day.
Butter was supplied as a control source of fatty acids in 10 g portions and patients were advised to take approximately one package within two days, i.e. 5 g daily, in addition to their usual diet. Since butter contains approximately 80% of fat, this dose approximately equals the daily dose of fatty acids administered with the n-3 PUFA capsules.

| | |
|---|---|
| Actual start date of recruitment | 27 August 2008 |
| 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 | Austria: 62 |
| Worldwide total number of subjects | 62 |
| EEA total number of subjects | 62 |

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) | 62 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment was performed at the General Hospital from the Medical University of Vienna in Vienna, Austria. Patients who were scheduled to undergo bariatric surgery were screened for inclusion and exclusion criteria. If patients seemed eligible for inclusion in the trial they were contacted by investigators for the trial ans asked to participate.

### Pre-assignment

Screening details:

Screening began in the summer of 2008 and a total of 148 patients were screened. Of these 54 patients did not meet inclusion criterial (mostly due to preexisting type 2 diabetes) and 32 patients declined to participate.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | n-3 PUFA |

Arm description:

Patients treated with Omacor

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

Dosage and administration details:

4 capsules per day

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

Arm description:

Control treated patients receiving butterfat

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

Dosage and administration details:

Butter was supplied as a control source of fatty acids in 10 g portions (Tiroler Teebutter) and patients were advised to take approximately one package within two days, i.e. 5 g daily, in addition to their usual diet. Since butter contains approximately 80% of fat, this dose approximately equals the daily dose of fatty acids administered with the n-3 PUFA capsules.

| **Number of subjects in period 1** | n-3 PUFA | Control |
|---|---|---|
| Started | 30 | 32 |
| Completed | 27 | 28 |
| Not completed | 3 | 4 |
| Adverse event, non-fatal | 3 | 4 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | n-3 PUFA |
| Reporting group description: | |
| Patients treated with Omacor | |
| Reporting group title | Control |
| Reporting group description: | |
| Control treated patients receiving butterfat | |

| Reporting group values | n-3 PUFA | Control | Total |
|---|---|---|---|
| Number of subjects | 30 | 32 | 62 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 30 | 32 | 62 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| 62 | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 25 | 25 | 50 |
| Male | 5 | 7 | 12 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | n-3 PUFA |
| Reporting group description: | |
| Patients treated with Omacor | |
| Reporting group title | Control |
| Reporting group description: | |
| Control treated patients receiving butterfat | |

### Primary: inflammatory gene expression

| | |
|---|---|
| End point title | inflammatory gene expression |
| End point description: | |
| Expression of inflammatory genes in adipose tissue at the end of the treatment was analyzed according to the delta delta Ct (ddCt) method, normalized to ubiquitin C, and expression levels were calculated as 2^(−ddCt). Data was presented as the mean (+/-SEM) of subcutaneous adipose tissue (SAT) from control subjects in percent. The mean of the SAT 2^(−ddCt) was set to 100%. | |
| End point type | Primary |
| End point timeframe: | |
| at the end of the treatment periode | |

| End point values | n-3 PUFA | Control | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 26 | | |
| Units: percent SAT control | | | | |
| number (not applicable) | | | | |
| CCL2 | 69 | 100 | | |
| CCL3 | 62 | 100 | | |
| IL6 | 45 | 100 | | |
| HIF1A | 78 | 100 | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Statistical analysis |
| Statistical analysis description: | |
| The statistical analysis included all patients who completed the trial and from which appropriate materials were obtained (n = 49) for adipose tissue and 55 for blood variables, except as otherwise indicated). Group differences between ddCt values in visceral adipose tissue (VAT) and SAT were analyzed by Student’s t test. Treatment effectiveness was considered achieved if statistical significance was demonstrated at the prespecified nominal a-level (0.05) for most of the primary endpoints. | |
| Comparison groups | n-3 PUFA v Control |

| | |
|---|---|
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| P-value | < 0.05 |
| Method | repeated measures ANOVA |
| Parameter estimate | time x treatment interaction |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| lower limit | 0 |
| Variability estimate | Standard error of the mean |

Notes:

[1] - A reduction of the primary outcome variable by 50% (corresponding to a change of +1.0 in dCt values. dCt is the logarithmic measure of gene expression analysis by quantitative real-time PCR normalized to a control gene) was considered clinically significant.

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: 2008-2011 | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 22 |
| **Reporting groups** | |
| Reporting group title | Diabetes |
| Reporting group description: 4 patients were diagnosed with new type 2 diabetes mellitus upon the OGTT performed at randomisation. They were subsequently excluxded from the trial. | |

| Serious adverse events | Diabetes | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | Diabetes | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| Endocrine disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 4 / 62 (6.45%) | | |
| occurrences (all) | 4 | | |

## 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.

The trial has been conducted between 2008-2011. Since then many years have passed but all data sets are available, thus it is easy to identify all relevant information. The data has been published in the American Journal of Clinical Nutrition.

Notes:

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/23034965