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
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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 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 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