Significant Weight Loss under formoline L112 in Overweight Patients with Type 2 Diabetes — A Multicenter Observational Study

Otto C, Stoll M, Heitmann C, Willms G, de Vries F, Trabold E, Grebe W, Jauniskyte A, Kaftanikiene D, Dobrovolskiene J, Antila E, Toukkola J, Ruuti M, Cserny M, Elčič-Mihaljević K, Heimayr C, Sock R, Pokhis K, Jung U, Kiefer I, Bitterlich N, Burkard I

The dramatic decline in the physical stresses experienced by each individual person is one reason for the worldwide increase in those who are overweight. An additional reason for this is the significantly improved food supply in all industrial nations of categories I and II. This resulting condition of socioeconomically caused changes in the food supply and minimal physical exertion has in the meantime been classified as a disease that requires treatment, namely as being overweight and/or obese with a high incidence of the metabolic syndrome.

For example in China it has been determined that the daily energy demand today has declined by up to 800 kcal versus the agrarian past. If such a situation does not result in a change or adaptation of nutritional habits, the development of overweight is almost unavoidable.

A gold standard for treating overweight and obesity could not yet be defined. Therefore, each therapist – in addition to recommending a change in eating habits and increased physical activity – must individually decide in which way the weight reduction measures for the patient should be supplemented. The medical device, formoline L112, is an aid with few side effects.

The reduction of fat intake from the intestinal tract as a result of „fat binders“ such as formoline L112 can support weight loss. Fat has the highest energy density; simultaneously, food in Western industrial nations also contains large daily quantities of up to 150 g fat. Specialist organizations recom-

mend reducing fat intake to 40 - 60 g per day to achieve a normal weight. However, without adequate quantities of fat eating becomes unattractive from the perspective of taste. This reduces nutritional discipline, frequently leads to „diet violations“ and finally results in frustration which initiates a return to old eating habits. In this situation formoline L112 could help to maintain discipline, since the permitted quantity of fat at about 80 g ensures that food is tasty. Thus, eating remains fun and also serves its social function of a commonly shared experience with family and friends.

The medical device formoline L112 has as its main ingredient a glucosamine-containing fiber, a ß-1,4 polymer composed of D-glucosamine and N-acetyl-D-glucosamine as an intestinally active lipid adsorber.

The polymer is an indigestible fiber or roughage which after passing through the intestinal tract is excreted in the natural way. After orally ingesting the active substance with 250 ml of a low-calorie liquid, the tablet dissolves in the acidic environment of the stomach. A solution results in the stomach, since protonation of the basic amino groups creates positively charged parts of the molecule.

In the slightly alkaline milieu of the intestine ß-1,4-poly-D-glucosamine is then deprotonated. The loss of charge reduces the hydrophilic profile of the compound; the polymer becomes nearly insoluble and its viscosity increases. In this form it serves as a lipid adsorber in the intestinal lumen; the adsorber is mixed with the chymus through intestinal peristalsis which facilitates its binding activities.

The active substance specifically binds a large quantity of bile acids, lipophilic substances and nutritional fats and thus prevents them from being absorbed. This mechanism removes the associated calories from the metabolism.

When properly used the product is taken twice daily at a dose of 2 tablets polyglucosamine for weight loss and then 2 x 1 tablets for weight stabilization over the long-term.

In the present observational study 50 percent of the documented overweight to obese study participants (BMI >26) received formoline L112 as a supplement to a course in nutrition. The course in nutrition with beha-

vioral training facilitates learning a fat-modified diet and through such a nutritional change to more easily achieve the desired weight loss as well as to stabilize the target weight over the long term.

The results of a multicenter, multinational, non-interventional study (NIT) will be reported below. This German observational study was started in 2006 and was initially only conducted in Germany by physicians in private practice. Initial results were available in February 2007. In the meantime the study will be continued on a multinational basis. The documentation was continued in Lithuania, then in Finland and Austria; Estonia started in 2008. Additional European countries are in the planning phase.

The biometric analysis analyzed the data from all of the study sites according to country, compared the data in a cross-national manner and then statistically analyzed the data within the overall study.

Study description

This staggered observational study documented the formoline nutritional course in overweight to obese patients and the simultaneous use of the medical device formoline L112 in approximately 50 percent of the participants. The remaining 50 percent of the study participants were either given the nutritional course exclusively or partially supported by placebo. In this way the formoline L112 group was compared with a standard therapy group.

With the assistance of the nutritional course, the patients were supposed to learn how to switch to a wholesome, low-fat diet. To this purpose, the therapists at the study sites in Germany were given the certified Medical Tribune Training Manual „Treatment of Obesity in Practice“ with detailed documentation on the nutritional course.

The recommendations contained therein are based on the pertinent guidelines of the German Society for Nutrition and the guidelines of the German Obesity Association. A translated version of the nutritional course was used in foreign countries.

In accordance with the protocol, each study site included an average of five patients per group in the documentation. The most important inclusion criteria for participating were a BMI > 26 and type 2 diabetes mellitus; the most important exclusion criteria were prior intestinal diseases or a change in intestinal function as well as a known hypersensitivity to crustaceans.

The observation period for each patient was 12 weeks.

Before conducting the nutritional course, we obtained the basic data concerning age, sex, height, weight, waist or hip measurement and blood pressure as well as the quality of life. Cholesterol and blood pressure values likewise should be recorded before the beginning and at the end of the documentation period. The first five patients per study site should be given formoline L112 and an additional five cases should achieve their weight loss with placebo or only with the support of the course and supervision by the therapist.

The course was split into 10 modules which each corresponded to an evening session lasting approximately 1.5 hours with the overall course lasting 10 weeks. Each of the modules provided comprehensive information on how to create a wholesome diet which contained moderate amounts of fat. Additionally, nutritional stimuli – also called „diet cases" – were discussed, nutritional and exercise behavior that supported weight loss was explained and within the group achievable goals for changing this behavior were established. Before the beginning and at the end of the course, an inclusion or exclusion examination was to be documented.

Approval of the Ethics Committee Frankfurt or approval in each of the countries participating in the study was obtained; patient insurance coverage to care for theoretically possible, serious adverse reactions was available.

Serious adverse reactions should be processed
according to the requirements of § 29 MPG; however,
they have not occurred so far.

Results

Biometric procedure:

All the variables in the collected data were exploratively analyzed and described by their key statistical figures (mean, standard deviation, median) or their frequency distributions. The statistical evaluation occurred by means of non-parametric bilateral tests. In the case of independent samples (group comparisons) the Mann-Whitney U-test was used; dependent samples (pre/post comparisons) were evaluated by the Wilcoxon test. The analysis of frequency distributions (percentage values) used the chi^2 test.

When comparing more than two samples, the non-parametric Kruska-Wallis test was initially performed. The subsequent paired comparisons were only performed on an explorative basis and are not corrected like multiple tests. Parametric test methods such as the t-test and variance analysis (ANOVA) complete the analysis and in all cases confirm the non-parametric test results.

The significance level was set at p-values up to 0.05. The statistical analysis was performed with the software suite SPSS® for WindowsTM, Version 12.

The collected data includes a total of 254 patients (status as of September 2008) from:

- Germany (105 patients from eight study sites, abbreviated as „De“ below),
- Lithuania (32 Patients from three study sites, abbreviated as „Lit“ below),
- Finland (27 Patients from three study sites, abbreviated as „Fin“ below),
- Austria (50 patients from four study sites, abbreviated as „A“ below) and
- Estonia (40 patients from three study sites, abbreviated as „Est“ below).

Plausibility test:

Fifteen (15) patients are excluded from the following analysis of the data:

- Six (6) patients from study site 5/De, because the duration of the study at 17 weeks was significantly longer than what was specified in the protocol,
- One (1) patient (No. 19) from study site 2/De due to discontinuation of the study at his own request,
- One (1) patient (No. 8) from study site 1 /A due to discontinuation of the study at his own request,
- Seven (7) patients from study site 4/A, because the duration of the study at 20 weeks was significantly longer than what was specified in the protocol.

Of the 239 remaining patients there are 15 patients (15 out of 239; 6.3 percent) who lost weight and exhibited a larger waist measurement, and nine patients (9 out of 239; 3.8 percent) who gained weight and exhibited a smaller waist measurement. In a total of seven of these cases (7 out of 239; 2.9 percent), the relative changes in the weight and the waist measurement did differ by more than four percentage points. These study results are considered to be implausible and are excluded from the study analysis.

Thus, the analysis includes a total of 232 patients
(232 out of 254; 91.3 percent).

Inclusion (date of the first visit) occurred in a time period from March 2006 until July 2008.

Country	Number Participant	Number Study Sites	Observation Period
total	232	21	09.03.06 – 11.07.08
De	96	8	09.03.06 – 11.07.08
Lit	32	3	14.03.07 – 03.07.07
Fin	27	3	05.04.07 – 28.09.07
A	42	4	14.09.07 – 30.01.08
Est	35	3	29.01.08 – 26.05.08

Table 1: Overview of the acquired data (according to country)

The study compares the use of formoline L112 at a daily dose of approximately 1.6 g versus a standard therapy with a nutritional course and partially with placebo. According to the allocation requirements, a total of 128 patients were assigned to receive formoline therapy (128 out of 232; 55.2 percent; called „F-group“ below), and 104 patients were assigned to receive the standard therapy (104 out of 232; 44.8 percent; called „S-group“ below).

Patient population:

The patients included in the study were on average 49.8 years old (± 13 years). The oldest patients came from Austria with an average age of 61.2 years (± 8.7 years) and the youngest patients came from Lithuania with an average age of 40.3 years (± 10.5 years). There were no statistically significant differences between the study groups with respect to age at baseline (p=0.496).

61 male and 171 female patients
participated in the study.

The average weight of the patients was 98.4 (± 20.4) kg with an average BMI of (34.6 ± 6.3) kg/m^2. At the beginning of the study, the patients in the F-group had an average weight of 100.9 (± 18.8) kg and those in the S-group a weight of 95.4 (± 21.9) kg. At baseline there were statistically significant differences between the study groups with regard to body weight (p=0.003), which were influenced by statistically significant weight differences in Lit (p=0.010). In the other countries distribution of the body weight in the study groups at baseline appears to be well-balanced, especially in De, A and Est (in each case P > 0.3).

At baseline there are statistically significant differences in the waist measurement (p=0.048) between the study groups, which are primarily determined by the (statistically not significant) differences in Lit (p=0.054). In all other countries the study groups are well-balanced with regard to the waist measurement (in each case p > 0.15).

Changes in the body weight:

Weight loss is statistically significant overall and in all countries ($p_{wil} < 0{,}001$).

Country	N	Patients Losing Weight		P-value (WIL-test)	Significance
		Number	Percentage		
total	232	208	89.7%	< 0.001	(✓)
De	96	89	92.7%	< 0.001	(✓)
Lit	32	28	87.5%	< 0.001	(✓)
Fin	27	23	85.2%	< 0.001	(✓)
A	42	37	88.1%	< 0.001	(✓)
Est	35	31	88.6%	< 0.001	(✓)

Table 2: Number/percentage of patients losing weight

The weight loss is statistically significant both in the F-group ($p_{wil} < 0.001$) and in the S-group ($p_{wil} < 0.001$).

		F-group			S-group		
Group	Number	Mean value	St.-Dev.	Number	Mean value	St.-Dev.	t-Test
total	126	4.2	3.0	106	2.8	2.5	0.000
De	53	4.7	3.2	43	3.3	2.8	0.025
Lit	16	4.9	3.3	16	2.9	2.5	0.055
Fin	15	3.9	3.0	12	2.2	2.4	0.106
A	22	3.6	3.2	20	2.8	2.4	0.385
Est	20	3.1	2.2	15	2.0	1.6	0.092

Table 3: Gewichtsabnahme nach Gruppen

The average weight loss of 4.2 kg in the F-group is greater than the average weight loss of 2.8 kg in the S-group ($p < 0.001$) in a highly significant statistical manner. In the participating countries the weight loss in the F-group is between 0.8 and 2.0 kg higher than in the S-group. Especially in De ($p=0.035$) and in Lit ($p=0.033$), the difference in weight loss is likewise statistically significant.

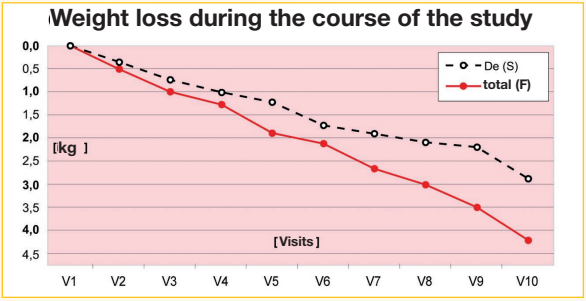

Fig. 1: Average weight loss during the course of the study

Comparison F-group/S-group with the percentage of specific responders (more than 4 kg or more than 5 percent)

Table 4: Responders (more than 5 percent)

	F-group		S-group		p-value
Group	Responder-percentage		Responder-percentage		Chi² test
total	36.5%	46 of 126	22.6%	24 of 106	0.022

The difference in the percentage of the responders exhibiting a weight loss of more than 5 percent versus the starting weight is at 36.5 percent in the F-group statistically significantly higher than in the S-group at 22.6 percent (p=0.022).

Results of a subgroup with bioelectric impedance analysis

At one German study site (No. 8) a bioelectric impedance examination of the body compartments was performed in addition to the observation plan applicable to all study sites. To this purpose we used the Inbody Data Management System, Biospace, USA.

This bioimpedance subgroup analysis included 14 patients who had their measurements taken both at visit 1 and also at the final visit. Of these

14 patients, eight patients (8 out of 14; 57.1 percent) were assigned to receive therapy with formoline L112 (abbreviated as „F-group“ below) and six patients (6 out of 14; 42.9 percent) were assigned to receive the standard therapy (abbreviated as „S-group“ below). The standard therapy included the use of a placebo.

The analyzed parameters included body weight, BMI, body fat percentage and mass as well as body cell percentage and mass. The percentage of patients with reduced values (body weight, BMI, body fat percentage and body fat mass) or increased values (body cell percentage and body cell mass) were more favorable in the F-group than in the S-group. This difference is statistically significant in the change of the absolute body fat mass.

With the exception of the absolute changes in body cell mass, all parameter alterations in the F-group were statistically significantly more favorable than in the S-group. The change in the absolute body cell mass is likewise consistent (statistically not significant) with these statements.

Parameter	F-group n= 8			S-group n = 6			
	Percentage with reduction	P-value (Wil.)	Mean change	Percentage with reduction	P-value (Wil.)	Mean change	P-value (U-test)
Body weight	87.5%	**0.036**	-3.5 kg	66.7%	0.917	+1.1 kg	**0.028**
BMI	87.5%	**0.036**	-1.3 kg/m²	66.7%	0.917	+0.3 kg/m²	**0.014**
Body fat percentage	87.5%	**0.017**	-2.9%	50.0%	0.833	+0.2%	**0.014**
Body fat mass	87.5%	**0.018**	-4.4 kg	33.3%	0.345	+0.8 kg	**0.005**

Table 5: Summary with parameter reductions in the F-group

Parameter	F-group n= 8			S-group n = 6			
	Percentage with increase	P-value (Wil.)	Mean increase	Percentage with increase	P-value (Wil.)	Mean increase	P-value (U-test)
Body cell percentage	87.5%	**0.017**	+1.9 %	50.0%	0.917	-0.2%	**0.014**
Body cell mass	62.5%	0.441	+0.5 kg	16.7%	0.345	+0.2 kg	0.699

Table 6: Summary with parameter increases in most chases

During the study, eleven patients (11 out of 14; 78.6 percent) in this group reduced their body weight.

These changes in the body weight are overall (p=0.086) and in the S-group (p=0.917) statistically not significant; however, statistical significance is seen in the F-group (p=0.028).

The F-group exhibits a weight loss of 3.5 kg on average. In contrast, a weight gain of 1.1. kg on average can be seen in the S-group.

Reduction in body weight [kg]	Number	Mean value	St.-Dev.
total	14	1.6	4.2
F-group	8	3.5	3.6
S-group	6	-1.1	3.7

Table 7: Reduction in body weight

The BCM percentage increased by 1.0 percentage points on average. The change in the BCM percentage is both overall (p=0.035) and also in the F-group (p=0.017) statistically significant; however, this is not the case in the S-group (p=0.917).

Increase in the BCM [%]	Number	Mean value[1]
total	14	1.0
F-group	8	1.9
S-group	6	-0.2

Table 8: Increase in BCM

Thus, the subgroup patients of the F-group have reduced their weight in a statistically significant manner and those in the comparison group have even gained weight. In the F-group the body fat mass was simultaneously reduced by 4.4 kg in twelve weeks while the comparison group exhibited an increase of 0.8 kg.

Likewise, the body cell percentage in the F-group had increased in a statistically significant manner while it had decreased in the comparison group.

This is also emphasized by the percentage increase of the BCM to 1.9 in the F-group while this value declined by 0.2 percent in the S-group.

This means that the weight loss in the F-group occurred at the expense of the body fat percentage.

Results of the total population continued:

BMI:

Overall, the BMI (consistent with the body weight) during the duration of the study declined in 208 patients (208 out of 232; 89.7 percent).

The decrease of BMI is statistically significant overall and in all countries ($p_{wil} < 0.001$). The BMI reduction was (1.2 ± 1.0) kg/m² on average. In the F-group the reduction was 1,5 kg/m² and in the S-group 1,0 kg/m² (p< 0,001).

There are statistically significant differences between the F-group and the S-group regarding the percentage of patients with a reduced BMI (p_{Chi}= 0,009).

Responders with more than a 1 kg/m² BMI decrease.

139 patients (139 out of 232; 59.9 percent) have reduced their BMI by more than 1 kg/m² versus visit 1 (baseline). 72 percent of the patients in the F-group and only 45.3 percent in the S-group have achieved this objective; this is statistically significant at p<0.001.

Changes in the waist measurement of all patients:

The average waist measurement reduction of 4.5 cm in the F-group is higher in a statistically significant manner than the average waist measurement reduction of 3.4 cm in the S-group (p=0.034).

Table 9: Waist reduction (absolute, in cm)

		F-group			S-group		
Group	Number	Mean value	St.-Dev.	Number	Mean value	St.-Dev.	t-Test
total	126	4.5	4.1	106	3.4	3.8	0.034

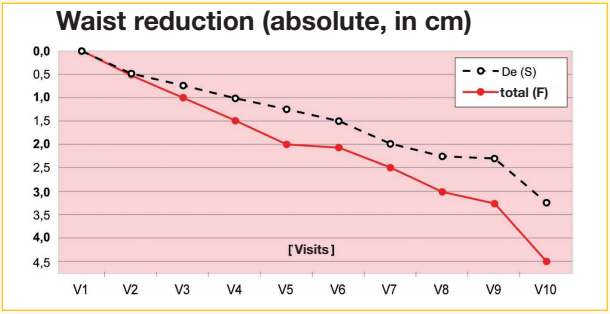

Fig. 2: Average waist reduction during the study

In De the difference is likewise statistically significant (p=0.031). Also in Lit, Fin and Est, the average reduction of the waist measurement in the F-group is between 0.9 to 1.7 cm higher than in the S-group. The opposite effect can be observed in A. It needs to be mentioned that at study site 2 of Dr. Karmen Elčič-Mihaljević 20 essentially multimorbid patients taking corresponding medications were included. Thus, the results in Austria could be somewhat skewed by this patient group.

Table 10: Responder (mehr als 5 Prozent)

	F-group		S-group		p-value
Group	Responder percentage		Responder percentage		Chi² test
total	33.3%	42 of 126	17.9%	19 of 106	0.008

The difference in the percentage of the responders exhibiting a waist reduction of more than 5 percent versus the starting waist measurement is at 33.3 percent in the F-group statistically significantly higher than in the S-group at 17.9 percent (p = 0.008).

Table 11: Waist reduction (relative, in % with respect to the baseline)

		F-group			S-group		
Group	Number	Mean value	St.-Dev.	Number	Mean value	St.-Dev.	t-Test
total	126	4.1	3.5	106	3.2	3.3	0.047

Also in terms of the waist measurement compared to the baseline, the reduction of 4.1 percent in the waist measurement in the F-group is statistically significantly higher than the reduction of 3.2 percent of the waist measurement in the S-group (p=0.028).

Additional results

At baseline there were statistically significant differences in the **blood glucose value** between the study groups. Especially in De, it is the mean blood glucose value in the F-group which is statistically significantly lower than in the S-group.

Nearly 70 percent of all the study participants reduced their blood glucose value. A higher rate of 73.1 percent was achieved in the F-group (not statistically significant) than in the S-group at 63.6 percent. The average reduction in the blood glucose value of 9.5 mg/dl in the F-group is not statistically significantly higher than the average reduction of the blood glucose value of 8.6 mg/dl in the S-group.

Compared to baseline there were statistically significant differences between the study groups in the **cholesterol value**, whereby essentially in De the average cholesterol value in the F-group was statistically significantly lower than in the S-group.

Compared to baseline there were statistically significant differences between the study groups in the **LDL Cholesterol value**, whereby essentially in De and in Est the average LDL cholesterol value in the F-group was statistically significantly lower than in the S-group.

Nearly 72 percent of all the study participants reduced their LDL cholesterol value. A higher rate of 78.3 percent was achieved in the F-group (not

statistically significant) than in the S-group at 65.2 percent. The average reduction in the LDL cholesterol value of 12.3 mg/dl in the F-group is not statistically significantly higher than the average reduction of the LDL cholesterol value of 6.7 mg/dl in the S-group.

More than 71 percent of all the study participants reduced their **systolic blood pressure value**. A higher rate of 72.5 percent was achieved in the F-group (not statistically significant) than in the S-group at 69.9 percent. The average reduction of the systolic blood pressure value of about 10.0 mmHg in the F-group does not differ in a statistically significant manner from the average reduction of about 10.4 mmHg in the S-group.

More than 64 percent of all the study participants reduced their **diastolic blood pressure value**. A higher rate of 66.1 percent was achieved in the F-group (not statistically significant) than in the S-group at 62.4 percent. The average reduction of the diastolic blood pressure value of about 4.6 mmHg in the F-group does not differ in a statistically significant manner from the average reduction of about 4.7 mmHg in the S-group.

Changes in the quality of life total score (SF36)

Summing up the individual values of the eight responses of the SF 36 questionnaire it can happen that they vary between eight points (all information indicates „severe impairment“) and 24 points (all answers indicate „no impairment“).

Compared to baseline there are no statistically significant differences in the total score of the SF36 between the study groups.

More than 68 percent of all study participants increased their SF36 total score. At 75.0 percent in the F-group, this was in a statistically significant manner more than the 59.7 percent in the S-group. The average increase of the total score by 2.2 points in the F-group is not higher in a statistically significant manner than the 1.6 point increase seen in the S-group. This results show an improvement of the quality of life.

Adverse events

During the study, an adverse event (AE) was documented in 38 patients (38 out of 232; 16.4 percent).

An AE affected 27 patients in the F-group (27 out of 128; 21.1 percent) and eleven patients in the S-group (11 out of 104; 10.6 percent).

There are statistically significant differences between the F-group and the S-group regarding the percentage of patients with an AE (p=0.031).

Table 12: AE, 46 occurrences (multiple designations are possible):

Adverse event	total (N = 46)	F-group (N = 35)	S-group (N = 11)
Constipation	20	15	5
Diarrhea	9	6	3
Nausea	3	3	
Rash	2	2	
Meteorism	2	2	
Salivation	2	2	
Allergic reaction	1		1
Increase in blood	1		1
Gastric spasms	1	1	
Rapid bowel	1	1	
Disturbed sleep due to a twinge in the stomach	1		1
Pain in the epigastrium	1	1	
Digestion problems	1	1	
Sensation of fullness	1	1	

The patient with the allergic reaction (No. 2, study site 5/De, S-group) and one patient with meteorism (No. 4, study site 5/De, F-group) stopped treatment, but still attended the final visit.

All of the documented symptoms were temporary and did not require any medical intervention. They can be clinically classified as disorders in the sense of well-being. The digestion problems were more frequent in the F-group

than in the comparison group. Constipation can be explained by a fluid intake that is too low while simultaneously increasing the ingestion of fiber, by changed eating habits and by formoline L112. Drinking too little is a frequently observed problem, especially in women. It is primarily the increased amounts of fiber as a result of introducing formoline L112 into the intestinal tract that change the composition of the intestinal bacteria. This promotes a temporary increase in gas-forming bacteria. The increased gas formation can lead to meteorism. After an adjustment phase, most users of Formoline L112 have regular bowel movements with a slight increase in stool volume and the meteorism abates.

Serious adverse reactions
were not reported.

However, as a whole these adverse reactions are by far nonviolent compared to those that can occur when using drugs to support weight loss; they are occasionally unpleasant, but generally temporary and harmless. Clinically they are without significance.

Discussion

In the meantime the international observational study has been conducted in five countries: Germany, Lithuania, Finland, Estonia and Austria. The 232 cases show analogous results to those in the last analysis with previously published data from 149 cases. The average weight loss of 4.2 kg in the F-group is greater than the average weight loss of 2.8 kg in the S-group ($p < 0.001$) in a highly significant statistical manner. The patients taking formoline L112 on average have lost about 50 percent more weight than the comparison group.

As was shown in a subgroup of 14 German patients undergoing bioimpedance analysis, the subgroup of patients in the F-group reduced their weight in a statistically significant manner and those in the comparison group even gained weight. The comparison group is too small to draw additional conclusions from the weight gain. In twelve weeks the body fat

mass in the F-group decreased by 4.4 kg while the body fat in the comparison group increased by 0.8 kg.

? Simultaneously, the body cell percentage in the F-group was statistically´significantly elevated; in contrast, it was relatively unchanged in the comparison group. This is also emphasized by the percentage increase of the BCM to 1.9 in the F-group while this value declined by 0.2 percent in the S-group.

Even if this subgroup is too small to draw a general conclusion, it is nevertheless possible to deduce that the weight loss in the F-group is likely primarily the result of a changed body fat percentage. During the same time period, the patients in the S-group also lost muscle mass in addition to fat mass. It is remarkable that significant results already can be obtained in such a small subgroup. It is planned that these results will be checked in a long-term study using a larger patient collective.

The average waist measurement reduction of 4.5 cm in the F-group is higher in a statistically significant manner than the average waist measurement reduction of 3.4 cm in the S-group (p=0.034). Thus, the cases in the formoline group reduced their waist measurement by 37 percent more than the comparison group.

The laboratory values of blood glucose, cholesterol and LDL were usually more strongly improved in the F-group than in the S-group, despite the fact that these improvements were usually not yet statistically significant. Also the quality of life parameters in the SF 36 documented a more pronounced improvement in the F-group, probably due to the significant weight reduction, than in the S-group. However, here too no significant values were obtained.

The adverse reactions are dominated by digestive problems. These abated in all cases without medical intervention and clinically they can be classified as a disturbed sense of well-being. One patient suffering from meteorism ended the study prematurely. Allergic skin reactions were reported in three cases: two in the F-group and one in the S-group. This led to the patient in the standard group discontinuing the study; a cause

of this allergic reaction was not found. The elevated blood glucose in one patient of the S-group could be due to a dietary error.

Serious adverse reactions have not been reported in this study.

Overall, the most recent results of this multicenter, multinational formoline L112 observational study also confirm that formoline L112 achieves a significant weight loss of 4.2 kg versus 2.8 kg in the comparison group. formoline L112 makes it easier to lose weight and is associated with a more significantly developed reduction of the waist measurement and an improvement of the body compartments as shown in the BIA subgroup versus the comparison group.

References

American Heart Association. Heart Disease and stroke statistics – 2005 Update. 2005. Dallas. TX: American Heart Association.

Appel L J et al. A clinical trial on the effects of dietary patterns on blood pressure. New England Journal of Medicine. 1997.3 3611174124.

Dallman Met al. Chronic stress and obesity: A new view of „comfort food". Proceedings of the National Academy of Sciences of the United States of America. 2003. 100:11696 – 11701.

Heilbronn L K Noakes M, Clifton PM. Effect of energy restriction, weight loss and diet composition on plasma lipids and glucose in patients with type 2 diabetes. Diabetes Care. 1999, 22:889-895.

James WPT The fundamental drivers of the obesity epidemic. Obesity Reviews. 2008.9,1: 643.

Peters A. The Selfish Brain – Neue Vorstellungen zur Pathogenese des metabolischen Syndroms. 42. Wissenschaftlicher Kongress der Deutschen Gesellschaft. Ernährung e.V. [New Ideas on the Pathogenesis of the Metabolic Syndrome. 42nd Scientific Congress of the German Society for Nutrition e.V.] (DGE. 17.18.03.2005).

Pi-Sunyer FX et al. Effect of rimonabant, a cannabinoid-1 receptor, blocker, on weight and cardiometabolic risk factors in overweight or obese patients : JAMA. 2006, 15; 295:761-75.

Richter W. Gesundheitsvorsorge und Phytotherapie mit ungesättigten Fettsäuren. Tatsachen und Projektionen [Healthcare and Phytotherapy with Unsaturated Fatty Acids. Facts and Projections]. Phytotherapie [Phytotherapy]. 2004. 1, 4: 943

Roth, E. Wechselwirkung zwischen Adipositas und dem emotionalen Zustand [Interaction Between Obesity and the Emotional State]. Aktuel Ernaehr Med [Current Nutritional Medicine] 2006.31:183488. Georg Thieme Verlag KG Stuttgart.

Rotthoff T., Scherbaum A. Pharmakotherapie der Adipositas [Pharmacotherapy of Obesity]. Aktueller Stand und Perspektiven [Present Status and Perspectives]. Arzneimitteltherapie [Drug Therapy] 2006. 24: 314-319.

Scheen AJ et al. Rimonabant improves cardiometabolic risk profile in obese or overweight subjects: overview of RIO studies. Rev Med Suisse. 2006. 23; 2, 76: 1916-23.

Stoll M. Fokussierte Therapie gegen viszerale Adipositas [Focused Therapy Against Visceral Obesity]? 2007. Der Bayrische Internist [The Bavarian Internist] 1/07.

Torgerson JS et al. XENICAL in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care. 2004, 27, 1: 155461.

Turnbaugh PI et al. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature. 2006 444.

Wirth A.: Adipositas – eine Krankheit [Obesity – A Disease]? CARDIOVASC. 2007. 7:28-34.

Wirth A. Die negativen Auswirkungen des Wohlstand in den Grif bekommen [Getting a Handle on the Negative Effects of Prosperity]. Internet instruction at :www.dgk.mg/cmeInternertbildung at :www.dgk.org/cme

Vague J. The degree of masculine differentiation of obesity: a factor determining predisposition to diabetes, atherosclerosis, gout, and uric calculus disease. Am J Clin Nutr.1956 4, 1:20-34.

Van Gaal LF et al. Effects of the cannabinoid-1 receptor blocker rimonabant an weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study. Lancet, 2005.365; 9468: 1389-97.