New Clinical Study Results
March 2010

Evaluation of ID-alG™'s weight-management effect on overweight women.

Monocentric, randomized, placebo controlled, in parallel double-blind format.

ABSTRACT

The aim of the clinical study was to confirm the weight-management properties of ID-alG™ on human and particularly on overweight women.
This clinical trial was a monocentric, randomized, placebo controlled study, conducted in parallel double-blind format. Sixty overweight or obese women (BMI between 28 and 39) were randomized in a parallel design into two groups of equal size (30 subjects per group).

During 8 weeks, half of the volunteers consumed 400mg of ID-alG™ (2 capsules) and the other half consumed a placebo at the same dose. The placebo capsule had the same size, same odor and same color (blue capsule) than the tested product, ID-alG™.

The efficiency of ID-alG™ was evaluated by non-invasive measurements performed at D0, after 4 weeks (D28) and after 8 weeks of treatment (D56). Blood samplings were collected at D0 and after 8 weeks. The evaluation was made by measuring body weight, body fat mass, body lean & water mass, circumferences, BMI.
To assess the safety of ID-alG™, liver transaminases (ASAT and ALAT) were measured before the study (at D0) and at the end (D56); no adverse event or modification of the transaminases blood rate was observed.

After 8 weeks of treatment, a moderate effect was observed on weight between the two groups on the *per protocol* population. This result was mainly due to the wide range of BMI covered by this per protocol population (from 28 to 39).
The focus on the sub-group of overweight women (BMI≤30) allowed to highlight the weight-management properties of ID-alG™ : the weight loss observed in the ID-alG™ group reached -2.8 kg after 8 weeks whereas women in the placebo group gained about 0.96 kg (p=0.047).
Regarding the product satisfaction, more than 70% of the subjects were convinced by ID-alG™ and would like to buy it to continue the treatment compared to 49% in the placebo group.

This clinical study, conducted in respect of all ethical and official principles for medical research with good clinical trial practices, ethics and statistical analysis, confirmed that ID-alG™ could help overweight women to lose weight and thus decrease their BMI.

Key words: weight-management, body weight, ID-alG™, overweight, BMI, weight loss

INTRODUCTION

ID-alG™ is a brown seaweed extract offering two complementary weight-management properties.
Preliminary studies highlighted that ID-alG™ inhibits lipase and amylase activities, and thus can help reducing fat and sugar absorption.
Moreover, thanks to its seaweed origin, ID-alG™ iodine content could help to increase thermogenic metabolism and fat reduction.
Until now, ID-alG™'s effect was only supported by *in vitro* and *in vivo* studies.

It is relevant to remind that the prevalence of obesity worldwide has progressively increased over the past decades. Obesity has reached epidemic proportions not only in the USA but also in European-developed countries. According to the National Health and Nutritional Examination Survey from 1988-1994 (NHANES III) to NHANES 1999-2000, the prevalence of overweight in adults *(Body Mass Index, BMI between 25.0 & 29.9 kg/m²)* increased from 55.9% to 64.5% and obesity *(BMI > 30kg/m²)* from 22.9% to 30.5% [Ogden CL, & al 2006].

Products already sold on the weight-management market act locally in the gastrointestinal tract to inhibit lipase, a crucial enzyme for the digestion of long-chain triglycerides (ex: Orlistat). At the recommended dose of 120 mg three times daily, Orlistat inhibits dietary fat absorption by about 30%. Over a 1-year period, obese patients taking Orlistat in combination with a hypocaloric diet show an average weight loss of 2-5kg compared to Placebo [Ballinger A, 2001]. But according to the FDA's Adverse Event Reporting System, 32 reports of serious liver injury, including 6 cases of liver failure, were submitted between 1999 and October 2008 in patients using Orlistat.

ID-alG™ is produced from *Ascophyllum nodosum* which is a marine seaweed traditionally consumed over decades. Thanks to its safe and natural origin, ID-alG™ does not present any adverse effect commonly associated with drug consumption. This key point confirms the interest of ID-alG™ as a natural alternative to reduce body weight without risk.

Based on this data, BIO SERAE recently invested to confirm ID-alG™'s weight-management properties on human and to reinforce ID-alG™'s scientific background.

The aim of the study was thus to assess the effect of ID-alG™ on body weight and fat mass evolution and confirm the hypothesis that ID-alG™ could help reducing the caloric intake, linked with the lipid and triglyceride metabolism.

1. Subjects & Method

1.1. INVESTIGATIONAL PLAN

This study was a monocentric, parallel, double-blind, placebo-controlled trial on overweight and obese women. Volunteers were randomized in a parallel design into two groups of 30 subjects.

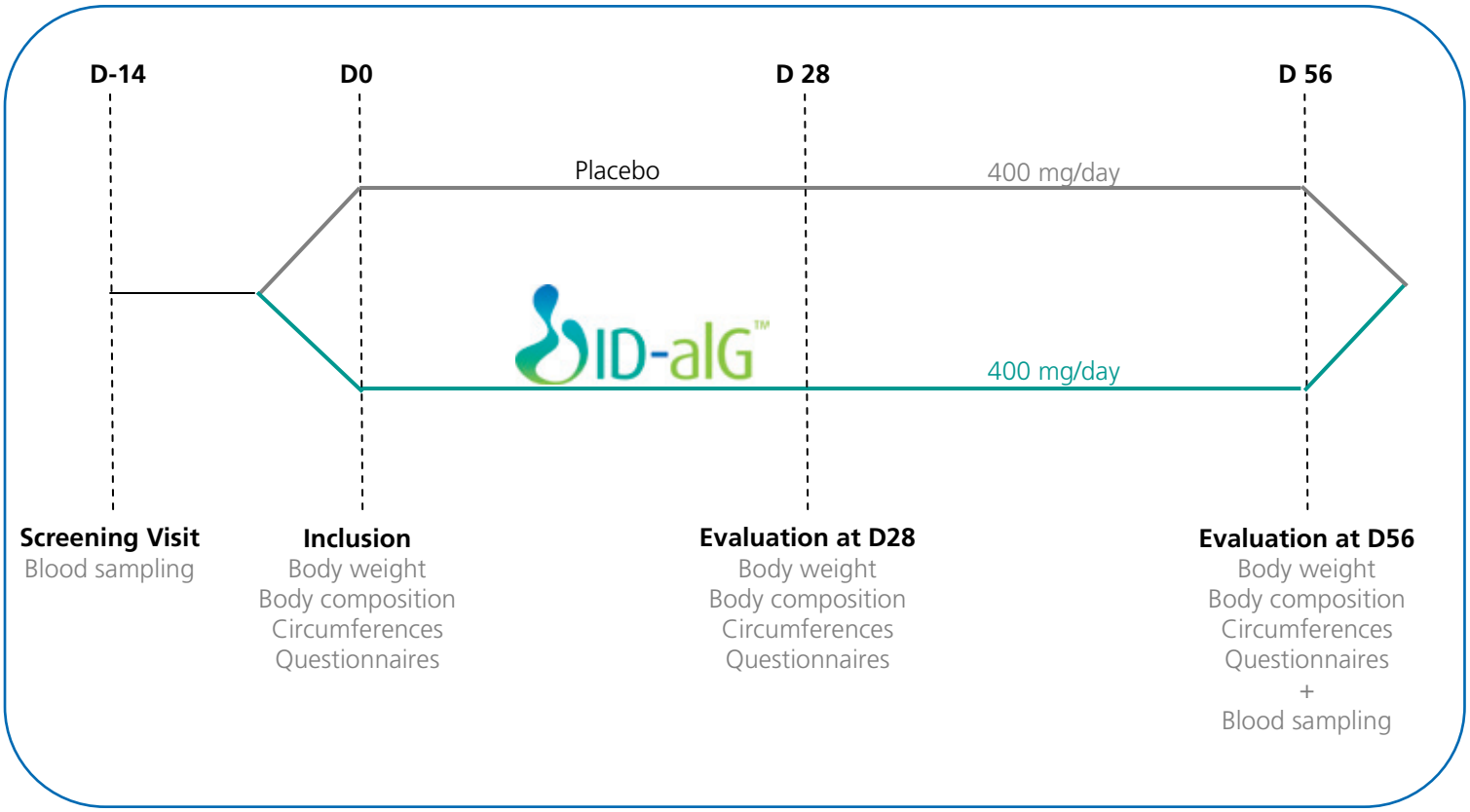
During 8 weeks, half of the volunteers consumed 400mg/day of ID-alG™ (2 capsules) and the other half consumed a placebo at the same dose.

The capsules were made to have the same size, same odor and same color (blue capsule) both for ID-alG™ and Placebo.

Non-invasive measurements (tape measure, impedancemeter TANITA® and subjective questionnaire) were performed at D0, after 4 weeks (D28) and after 8 weeks of treatment (D56). Blood samplings were collected at D-14 (screening visit) and after 8 weeks.

Subjects estimated their diet every week and performed moderate level of exercise (daily walking for 20 minutes) during the study period.

FLOW CHART of the study.



Schedule	Visit 1 Screening	Visit 2 Inclusion	Visit 3 Evaluation	Visit 4 Evaluation
Days	**D-14 max**	**D0**	**D28**	**D56**
Informed consent signature	■			
Medical examination	■			■
Medical history	■			
Previous or concomitant medications	■			
Checking of the inclusion and non-	■	■		
Blood sampling (TSH and HBA1c	■			
ECG	■			
Body Mass Index	■	■	■	■
Blood sampling (transaminase level analysis)	■			■
Inclusion		■		
Impedancemetry parameters		■	■	■
Centimetric measurements		■	■	■
VAS Hunger and satiety		■	■	■
Dispense study material + daily diary		■	■	
Collect unused study material			■	■
Diet recording		■	■	■
Self-Assessment				■
AE collection		■	■	■
Concomitant treatments collection		■	■	■
Study end				■

Table 1: Visit procedure

Visit procedures details

Visit 1: Screening visit :

> Volunteers were informed orally about the study aims, restrictions and risks, and then, read the information notice and consent form. If they agreed to participate in this study, volunteers signed the informed consent form in duplicate.
> The investigator conducted a medical examination with an ECG to check that the global health state of volunteers allowed them to begin this study and that they met all inclusion and exclusion criteria, including the body mass index calculation.
> A blood sample was taken to check TSH, HbA1c and transaminases blood level.
> The volunteers filled in the diet questionnaire.

Eligible volunteers were given the next appointments as well as the study recommendations.
If blood analysis were abnormal, the subject could not participate in the study. The investigator contacted her for a consultation at DERMSCAN and orientated the subject to her usual practitioner or to an appropriate specialist.

Visit 2: Inclusion or D0 :

> The investigator checked if each volunteer still corresponds to the criteria to confirm her inclusion in the study. All the adverse events and/or concomitant treatments occurred since the last visit was registered.

Then, several evaluations were done:

- Measurements of hips, buttocks and thighs circumferences,
- Measurement of impedance parameters (weight, body fat mass, BMI and body lean mass) with TANITA® impedancemeter.
- Auto-evaluation of hunger and satiety on Visual analogical scales.

> Product distribution according to the randomization list.
> Each volunteer received a diary to fill in each day in order to record her diet and note the daily consumption of the products, the possible intolerance sensations and the treatments taken during the study, if any.

Visit 3 : After 4 weeks treatment (D28):

> Return of the diary fully completed, the unused products and the diet questionnaires.
> Adverse events and concomitant treatments recording.

Then, several evaluations were done:

- Measurements of hips, buttocks and thighs circumferences,
- Measurement of impedance parameters (weight, body fat percentage, BMI and lean body mass) with TANITA® impedancemeter.
- Evaluation by the subject of hunger and satiety on Visual analogical scales.

> Product distribution according to the randomization list attributing the treatments
> Each volunteer received a diary to fill in each day in order to record the diet and note the daily consumption of the products, the intolerance sensations felt and the treatments taken during the study if any.

Visit 4 : After 8 weeks treatment (D56):

> Return of the diary fully completed, the unused products and the diet questionnaires.
> Adverse events and concomitant treatments recording.
> Blood samplings.
> The investigator conducted a medical examination with an ECG to check that the global health state was unchanged.

Then, several evaluations were done:

- Measurements of hips, buttocks and thighs circumferences,
- Measurement of impedance parameters (weight, body fat percentage, BMI and lean body mass) with TANITA® impedancemeter.
- Evaluation by the subject of hunger and satiety on Visual analogical scales.

1.2. POPULATION

Each group was assigned with a code which was known only by the nominated statistician and was only broken at the analysis stage of the study, unless a serious adverse event occurs. At any time of the study, neither the investigator, nor the volunteers knew the nature of the product used (ID-alG™ or placebo).

Among the 79 patients pre-included in the study, 19 subjects were not randomised.
Finally, 60 subjects were divided in two groups and received either the placebo or ID-alG™ capsules.

- one group received the product ID-alG™ (N=30 at the beginning and N=25 at the end of the study (5 persons were dropped out during the blind review due to external events)
- One group received the placebo (N=30 subjects at the beginning and N=29 at the end of the study (one subject was dropped out during the blind review for similar reason).

During the study, 6 volunteers dropped out (4 at D0 and 2 at D28).

Table 2 –Distribution of volunteers in the Per Protocol population

	Product	Between D0& D28	Between D0 & D56
Per Protocol population	Total	N=56	N=54
	ID-alG™ group	N=26	N=25
	Placebo group	N=30	N=29

1.3. DEMOGRAPHIC CHARACTERISTICS

1.3.1. Total population

Details of the demographic characteristics are summed up in the following table (Table 3).

Table 3 – Synthesis of the general characteristics of women included

Group	Number	Age (average ± SD)	Height in cm (average ± SD)	Weight (average ± SD)	BMI (average ± SD)
total population	60	33 ± 1 (19 < age <45)	162 ± 1	86.7 ± 1.2	32.8 ± 0.3
ID-alG™	30	34 ± 1	163 ± 1	87.4 ± 2.0	32.9 ± 0.2
Placebo	30	32 ± 1	162 ± 1	86.0 ± 1.5	32.7± 0.4

1.3.2. BMI range Sub-groups

In the Per Protocol population, the weight was comprised between 69.2 kg to 112.5 kg, leading to a wide range of BMI from 28 to 39.
The analysis of the population showed a heterogenous repartition between the different ranges of BMI (25 to 30; 30 to 35 and 35 to 39).
Most of the women were in the middle range (30-35), meaning already in an obesity status.

The subject distribution in the sub-groups of BMI is summarized in the Table 4.

Table 4 – Sub-groups distribution according to BMI

	Total Population		
	ID-alG™ Group	Placebo Group	TOTAL
BMI between 25-30	4	5	9
BMI between 31-35	22	22	44
BMI between 35-39	5	3	8
Total	30	30	60

1.3.3. Analysis of the initial HbA1c

HbA1c is a biologic criteria used to evaluate the glucose metabolism during the 3 previous months. HbA1c is like a picture of the diet intake on a 3 months period. A HbA1c rate of 6.0 is considered as a diabetes indicator.

According to the protocol, the HbA1c was measured at the beginning of the study (D0).
Due to the exclusion criteria (exclusion of diabetic subjects), no women were higher than 6.0 and the lowest level was at 5.1.
In the *Per Protocol* population, 37 women had a HbA1c rate comprised between 5.0 and 5.5, and 23 women had a HbA1c rate higher than 5.5, meaning that they could have a risk to become diabetic in the future.

Table 6: Subject distribution according to HbA1c rate at D0

Range of HbA1c	Number of women		
	ID-alG™ Group	Placebo Group	Total
5.0 – 5.5	17	20	37
5.5 – 6.0	13	10	23
Total	30	30	60

1.4. PRODUCTS & TREATMENTS

Each volunteer received either the tested product (ID-alG™) or the placebo in a capsule form (200mg/capsule).
The placebo and ID-alG™ capsules have the same size, same odor and same color (blue capsule).

The products were presented in sealed boxes containing the required quantity (66 capsules per box) to cover the 4 weeks dosage between 2 visits to the laboratory.

The recommended dosage is two capsules per day, one capsule per each of the main meals (lunch & diner).

1.5. STATISTICAL ANALYSIS

The statistical analysis was performed after the database was cleaned and judged valid. The database was then locked.
The statistical analysis was made in blind. No interim statistical analysis was performed. The safety analysis was performed on the safety population.
The efficacy analysis was performed on the *Per Protocol* population and on sub-groups (dietary intake or BMI).

The statistical analysis was made to evaluate the slimming effect of the tested supplement versus placebo and was performed on the following parameters:

- Measurements of thighs, hips and buttocks circumferences.
- The impedance parameters for entire body (weight, impedance, water mass, lean and fat mass and BMI),
- The hunger and satiety feelings using visual analogical scales filled in by the subjects,
- Subjective questionnaire to evaluate the organoleptic characteristics and efficacy of the tested product,
- General safety of the product thanks to the evaluation of adverse events collected during the study.

Each parameter of the evaluation criteria (circumferences, impedance parameters, hunger and satiety feelings) was described for each treatment group and each kinetics time by average, median, minimum, maximum and standard deviation.
The variations between D28-D0 and D56-D0 of each parameter was entered, described by treatment group and summarized by mean, median, minimum, maximum, IC95% and standard deviation.
The comparisons of variations observed during the 2 periods D28/D0 and D56/D0 and between treatment groups (tested product and placebo) were performed using a Student T-test or an equivalent non parametric test if the normality condition was highly violated.

The organoleptic characteristics and efficacy of the product evaluated by a subjective questionnaire was described and summarized by treatment groups and kinetics time by the frequency and percentage for each response category (n, %).

General safety data (all Adverse Events / Serious Adverse Events) collected during the study were listed and tabulated by treatment group.

All statistical tests were assessed at the 5% level significance and where applicable, the two-tailed approach was used.
The software of the statistical analysis was SAS® version 9.1.

2. Results on the *Per Protocol* population

For the *Per Protocol* population, both product groups (group product vs group placebo) were homogeneous in term of baseline values, whatever the parameter was (no significant difference between the two groups).

This population is divided as follows:

For the first period (D0-D28):
- Placebo Group: N=30
- ID-alG™ Group: N=26

*Statistical analysis of the results between D0 and D28 on this per protocol population are conducted **on N=56**.*

For the second period (D28-D56):
- Placebo Group: N=29
- ID-alG™ Group: N=25

*Statistical analysis of the results between D0 and D56 on this per protocol population are conducted **on N=54**.*

2.1. VARIATIONS OF THE BODY WEIGHT

After 28 days of treatment, in the Placebo group, the weight tended to slightly increase whereas it did not vary in the ID-alG™ group.
However, the difference between the two products was not statistically significant.

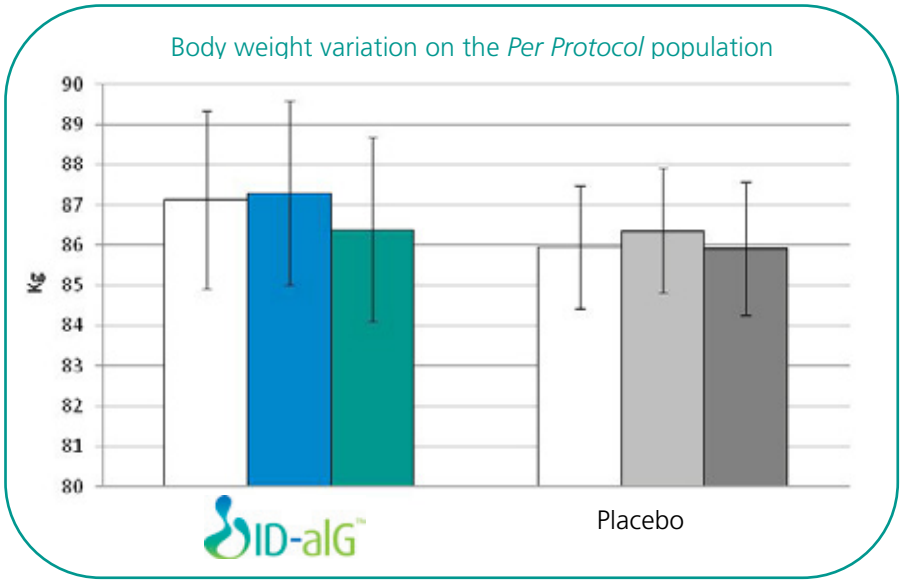
After 56 days of treatment, the average body weight of women in the ID-alG™ group was lower at D56 than it was at D0.
No significant difference was observed between the two products in this population.

Table 7: Body weight between D0 & D56

Product	D0	D28	D56
Placebo	85.96 ± 1.53	86.37 ± 1.55	85.93 ± 1.65
ID-alG™	87.13 ± 2.22	87.29 ± 2.29	86.4 ± 2.28

Table 7bis: Body weight variation between D0-D28 & D0-D56

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	**0.41 ± 0.21**	0.4809	0.02 ± 0.31	0.8224
ID-alG™	0.17 ± 0.29		-0.22 ± 0.42	



Graph 1: Body weight variation between D0, D28 & D56

This clinical study began in the middle of December 2009 and each volunteer was involved for a two months period. For each volunteer, the first part of this study was closely linked with the period of Christmas and New Year celebrations.

During this first period, it is then probable that these women had eaten more than usual, both in quantity and in quality (hypercaloric diet).
It is interesting to observe that in the *Per Protocol* population, women in the ID-alG™ group increased their weight by only few grams between D0 & D28 (+170g), whereas in the same period, women in the Placebo group increased a little more their body weight (400g).

2.2. VARIATIONS OF THE BMI (BODY MASS INDEX)

After 28 days, the BMI of volunteers in the Placebo group tended to slightly increase whereas the BMI of volunteers in the ID-alG™ group did not vary.
However, the difference between Placebo and ID-alG™ was not statistically significant.

After 56 days, no significant variation was observed between Placebo and ID-alG™.
This tendency could be explained by the large heterogeneity of the population: it was very difficult to have a strict statistical difference between both groups.

Table 8: BMI variation between D0 & D56

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	**0.16 ± 0.08**	0.5452	-0.02 ± 0.12	0.7052
ID-alG™	0.02 ± 0.14		-0.09 ± 0.16	

2.3. VARIATIONS OF THE BODY FAT MASS

Table 9: Body fat mass between D0 & D56

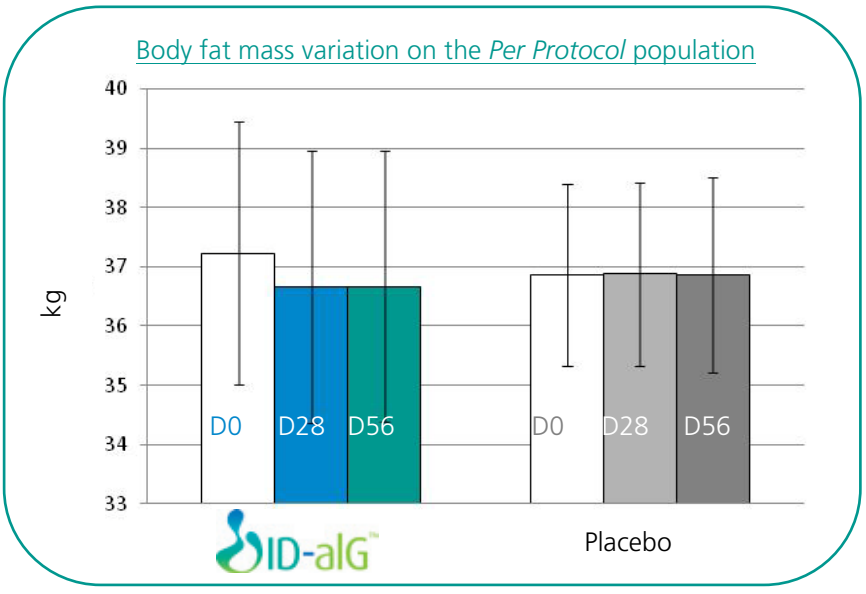
Product	D0	D28	D56
Placebo	36.86	36.88	36.87
ID-alG™	37.23	36.66	36.67

After 28 days of treatment, the body fat mass of women in the ID-alG™ group tended to decrease. The placebo did not induce any variation of the fat mass.
The difference between the effects of the two products was not statistically significant.

After 56 days of treatment, the fat mass decrease observed in the ID-alG™ group is lower than the one observed in the first period of the study (D0-D28).
The difference between the effects of the two products was not statistically significant.

Table 9bis: Body fat mass variation between D0 & D56

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.02 ± 0.23	0.1959	-0.12 ± 0.29	0.5981
ID-alG™	-0.57 ± 0.39		-0.25 ± 0.65	



Graph 2: Body fat mass variation between D0, D28 & D56

A fat mass loss was observed between D0 and D28 in the ID-alG™ group but it was not maintained during the second period.
In the placebo group, the body fat mass appeared to be unchanged at D0, D28 or D56.

The *per protocol* population covering a large BMI range (between 28 to 39) is considered as an heterogeneous population. That is why it is very difficult to highlight in this study a significant difference between women treated or not.

2.4. VARIATIONS OF THE BODY WATER MASS AND BODY LEAN MASS

After 56 days of use, no significant variation of the water and lean mass was observed on average, whatever the product consumed. The difference between the effects of both products was not statistically significant.
These results are in agreement with the results of weight and fat mass in the *per protocol* population.

Table 10: Body water mass variation between D0 & D56

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.29 ± 0.14	0.3540	-0.08 ± 0.17	0.7913
ID-alG™	0.54 ± 0.23		0.02 ± 0.31	

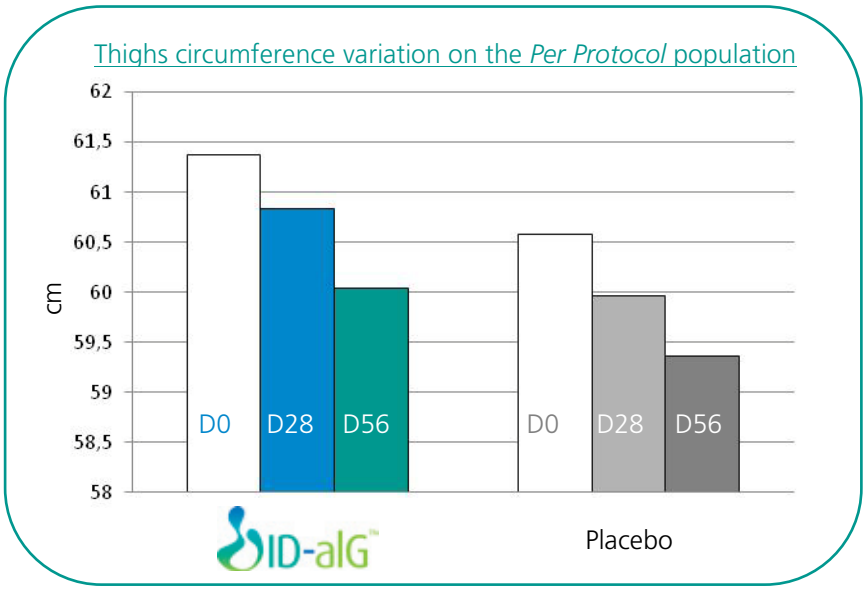
Table 10bis: Body lean mass variation between D0 & D56

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.39 ± 0.18	0.5452	-0.11 ± 0.24	0.7052
ID-alG™	0.74 ± 0.31		0.04 ± 0.43	

2.5. VARIATIONS OF THE CIRCUMFERENCE PARAMETERS

- Thighs circumference

After 28 and 56 days of use, both products induced a significant decrease in the thigh circumference. However, the difference between the two products was not statistically significant.



Graph 3: Thighs circumference variation between D0, D28 & D56

Table 11: Thighs circumference variation between D0 & D56

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	-0.61	0.72	-1.00	0.85
ID-alG™	-0.54		-1.06	

- Hip circumference

After 56 days, a significant increase in the hip circumference was observed for both the tested product and placebo. The difference between the effects of both products was not statistically significant.

Table 12: Hip circumference between D0 & D56

Product	D0	D28	D56
Placebo	105.03	105.35	106.22
ID-alG™	105.21	106.04	106.22

- Buttocks circumference

After 28 and 56 days of use, no significant variation of buttocks circumference was observed on average, whatever the product used.
The difference between the effects of both products was not statistically significant.

Table 13: Buttock circumference between D0 & D56

Product	D0	D28	D56
Placebo	115.89	115.79	115.41
ID-alG™	116.24	116.12	115.98

2.6. HUNGER AND SATIETY SCALE

After 28 or 56 days of treatment, no significant difference was observed between Placebo and ID-alG™ on the hunger score.

Table 14- Variations of the hunger score between D0-D28 & D0-D56

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.33 ± 0.26	0.2851	0.72 ± 0.29	0.6127
ID-alG™	0.88 ± 0.37		0.32 ± 0.30	

After 28 and 56 days of use, no significant variation of the satiety score was observed, whatever the product used.
The difference between the effects of both products was not statistically significant.

Table 15- Variations of the satiety score between D0-D28 & D0-D56

Products	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.43 ± 0.31	0.2748	0.07 ± 0.38	0.2634
ID-alG™	-0.12 ± 0.39		-0.56 ± 0.40	

2.7. QUESTIONNAIRE OF SATISFACTION

At the end of the study, each volunteer filled in the satisfaction questionnaire.
Results are presented here-after.

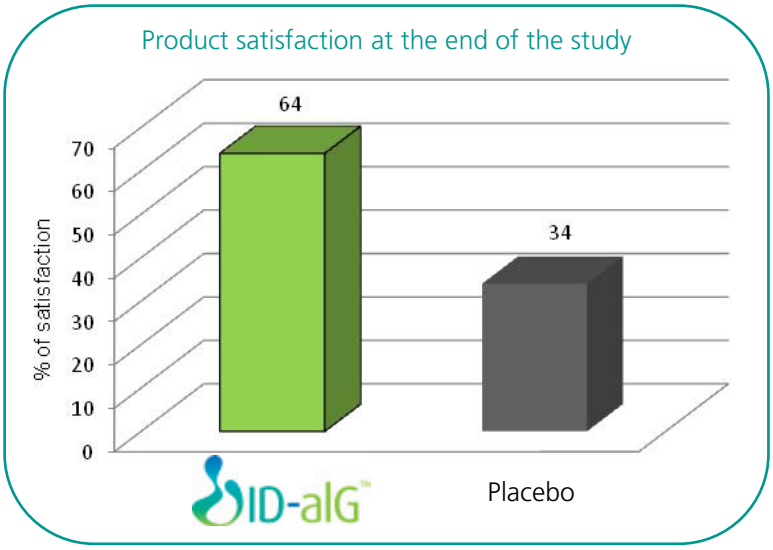
Table 16- Questionnaire results

	% of satisfaction	
	ID-alG™	**Placebo**
PRODUCT ACCEPTATION		
Q1- Global appreciation	**64%**	**34%**
Q2- Ideal capsule size	80%	83%
Q3- Capsule colour	56%	37%
Q4- Caspule taste	20%	24%
PRODUCT EFFICACY		
Q5- Limitation of weight intake or induction of weight loss	**76%**	**61%**
Q6- Slimming effect	**56%**	**34%**
Q7- Increase of intestinal transit	76%	58%
Q10- Sensation to eat less	80%	68%
Q11- Sensation to be less hungry	76%	62%
PRODUCT TOLERANCE		
Unpleasant or uncomfort sensations	12%	3%
PRODUCT FUTURE USE		
Q17- Would like to continue to use the product	**72%**	**45%**
Q18- Would like to buy the product	**72%**	**49%**

Considering the *per protocol* population size, the appreciation difference between the two groups should be higher than 20% to be considered significant.

2.7.1. Global appreciation

64% of the women in the ID-alG™ group are satisfied with the product effect.
Only 34% of the volunteers in the placebo group are positively satisfied, meaning that the percentage of women in that group is close to the placebo effect.



Graph 4: Product satisfaction

The difference of appreciation between the two groups, is about 30% (64% vs. 34%), which is considered a very positive result for ID-alG™.

2.7.2. Satisfaction linked to the weight-management effect

56% of women treated with ID-alG™ appreciated its slimming effect versus only 34% of satisfied women in the placebo group.

2.7.3. Global product tolerance

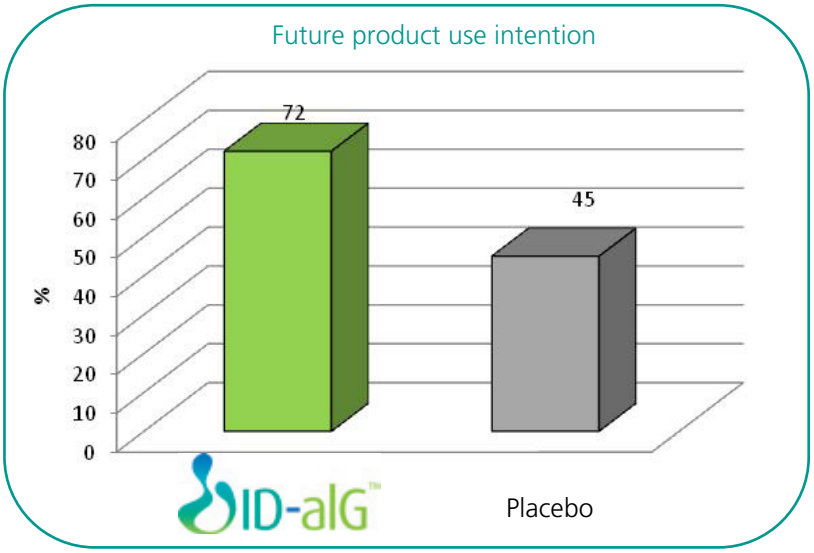
In the *Per Protocol* population, most of the women did not feel any serious side effect: 100% of the volunteers respected the treatment during all the clinical trial period.

More precisely, 88% of the women in the ID-alG™ group had a positive global product tolerance; only 12% had noticed some unpleasant or uncomfortable sensations probably linked to the increase of the intestinal transit.

2.7.4. Product future use intention

In the global appreciation, we asked to the *Per Protocol* population, if they would like to continue using the product (ID-alG™ or placebo product).

More than 70% of women included in the ID-alG™ group, declared that they would like to continue to use the product, whereas they were only 45% in the placebo group



Graph 5: Future product use intention

There is a sensible difference between "*would like to continue a treatment*" and "*would like to buy the product to continue the treatment*". The last question suggests an additional motivation linked with money.

Analysis of the questionnaire showed that 72% of women in the ID-alG™ group would like to buy the tested product whereas only 49% in the Placebo group.

2.8. SAFETY ON TRANSAMINASES (ASAT AND ALAT)

Transaminases analysis (ASAT and ALAT) were performed at the beginning and at the end of the study. The goal of this blood analysis was to give the proof that ID-alG™ is a safe product without adverse effects on the liver, especially on the transaminase levels which are markedly increased with another product present on the market; Alli® (orlistat).

Last year, the product Alli®, which is dedicated for weight-management especially for obese people, was allowed for sale without medicine prescription. However, few months later, several adverse events including liver injury appeared to be linked with Alli® treatment.

As the mechanisms of ID-alG™ tend to be the same as Alli® (lipase inhibition), Bioserae decided to check this safety point with a blood analysis on the ASAT and ALAT levels.

- Aspartate transaminase (AST) also called Serum Glutamic Oxaloacetic Transaminase (SGOT) or aspartate aminotransferase (ASAT) is an enzyme associated with liver parenchymal cells. Its level increases in case of acute liver damage among in liver, but also in red blood cells, and cardiac and skeletal muscle (no specific to the liver).
- Alanine transaminase (ALT), also called Serum Glutamic Pyruvate Transaminase (SGPT) or Alanine aminotransferase (ALAT) is another enzyme present in hepatocytes (liver cells). When a cell is damaged, it spreads this enzyme into the blood, where it can be measured. ALT dramatically increases in acute liver damage, such as viral hepatitis or paracetamol (acetaminophen) overdose.

Table 16- Results of Transaminases analysis

	ASAT (UI/l)		ALAT (UI/l)	
Product	**D0**	**D56**	**D0**	**D56**
Placebo	23 ± 1	21 ± 1	32 ± 2	42 ± 2
ID-alG™	23 ± 2	20 ± 2	32 ± 2	40 ± 2

On average, the ASAT levels did not change during the study, neither in the ID-alG™ group nor in the placebo group.

The ALAT slightly increased but in the same way in both groups. This increase is consequently not related to the tested product.

The transaminases ALAT and ASAT were not modified by the product ID-alG™ either.

Conclusion on the *Per Protocol* population

In the *Per Protocol* population, a slight increase in the weight and the BMI was observed with the placebo after 28 days (+400 g on average, variation at the limit of significance), whereas the weight and the BMI did not significantly changed in the ID-alG™ group.

After 56 days of use, the weight of women in the ID-alG™ group was lower than the weight at D0, but this average variation observed was not significant certainly due to the heterogeneity of the population. However, this difference was too weak to highlight a statistical difference between product and placebo.

In conclusion on the total population (*Per Protocol* analysis), no significant difference on the weight was highlighted between the effect of ID-alG™ and placebo.

Regarding the other parameters, some significant variations were observed in both groups: decrease in thigh circumference after 28 days and after 56 days, increase in water and lean mass after 28 days.
However, these variations were similar with the product and the placebo.

Concerning the satisfaction questionnaire, ID-alG™ was appreciated by 64% of the subjects whereas the placebo was appreciated by only 34% of the subjects. 72% of the subjects would like to continue using ID-alG™ against only 45% in the Placebo group.
Regarding the weight-management product efficacy, 56% of the subjects having used ID-alG™ were satisfied, against 34% with the Placebo.

The body weight of volunteers in the *Per Protocol population* was comprised between 69.2 kg and 112.5 kg, leading to a wide range of BMI from 28 to 39. The *Per Protocole* population can be thus classified in three categories: 28 to 30; 30 to 35 and 35 to 39). Most of the volunteers are in the middle range (30 to 35), which means they are already in an obesity status.

Results analysis was thus performed on the different BMI sub-groups and more particularly on the sub-group BMI<30, which corresponds to overweight people, one of the main targeted categories for ID-alG™.

3. Results on the sub-group with BMI between 28 and 30

The sub-group of volunteers with a BMI ≤ 30 was composed of 9 persons: 4 women in the ID-alG™ group and 5 in the Placebo group.

In this sub-group, significant differences were observed on several parameters between ID-alG™ group and Placebo group at the end of the study.

3.1. BODY WEIGHT VARIATIONS

In the ID-alG™ group, a weight reduction was initiated between D0 and D28 and was confirmed during the second part of the study, reaching a significant average weight loss of 2.8kg between D56 and D0.

In the Placebo group, the body weight slightly increased (+0.96 kg) between D0 and D56
The difference between the two groups was significant (p=0.0474)

Table 17: Body weight between D0 & D56 / Sub-group BMI<30

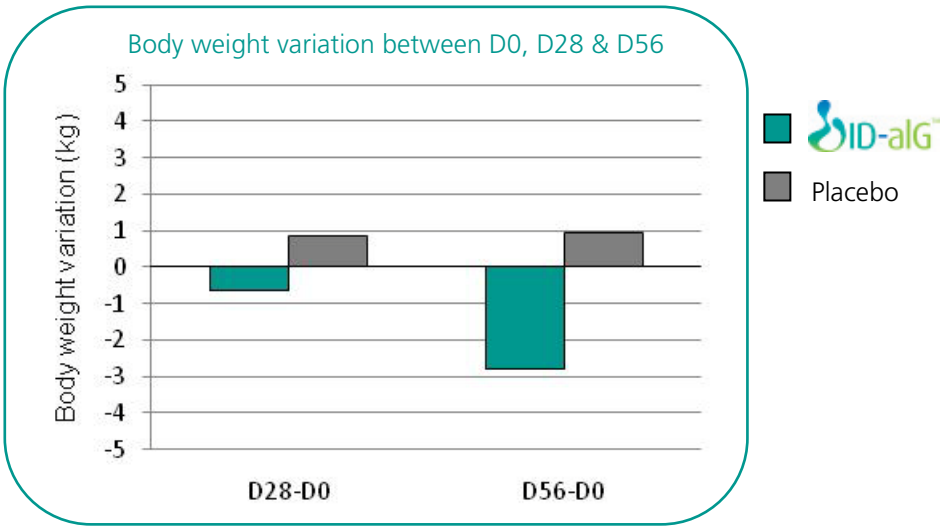
Product	D0	D28	D56
Placebo	77.02	77.88	77.98
ID-alG™	84.68	84.03	81.88

Table 17bis: Body weight variation between D28-D0 & D56-D0

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.86 ± 0.50	0.0870	0.96 ± 0.47	0.0474*
ID-alG™	-0.65 ± 0.57		-2.80 ± 1.68	

** p-value product vs. placebo (equal variances) p=0.0474*
p-value product vs. placebo (unequal variance) p=0.1071
The p for the variance equality is 0.0498, thus both p-values could be used for this parameter.

Graph 6: Body weight variation between D0 & D56 / Sub-group BMI<30



3.2. BODY MASS INDEX (BMI) VARIATIONS

As significant body weight variations were observed during the study, it was expected to observe some variations on BMI.

The difference between the two groups was at the limit of significance at D28 (p=0.0900) and became significant at D56 (p=0.0376).

Table 18: Body Mass Index variations between D28-D0 & D56-D0 / Sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.32 ± 0.19	0.0900	**0.34 ± 0.17**	0.0376
ID-alG™	-0.22 ± 0.21		**-0.90 ± 0.51**	

3.3. VARIATIONS OF THE FAT MASS & BODY FAT MASS PERCENTAGE

Variation of the fat mass

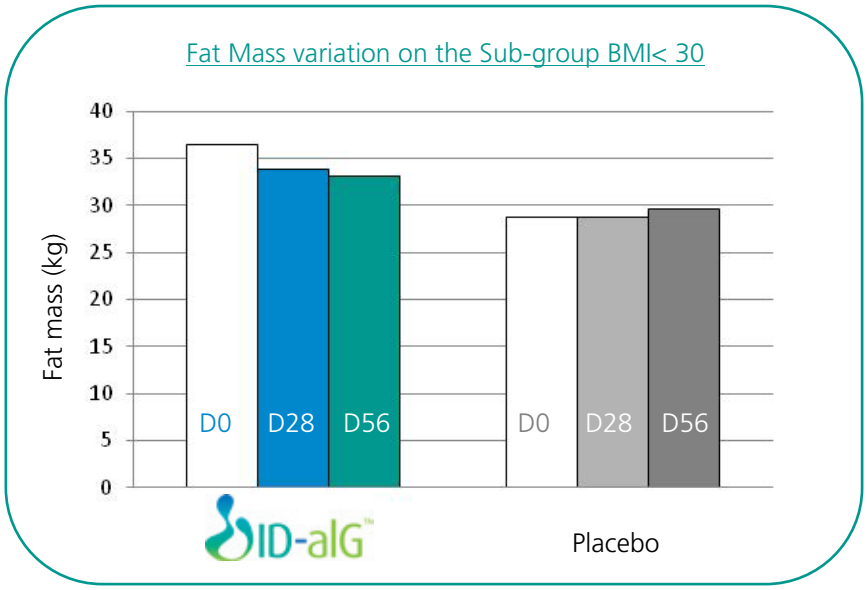
For this sub-group (BMI ≤ 30), fat mass values at D0 were significantly different between ID-alG™ and placebo groups:

- The average of fat mass in the ID-alG™ group was 36.3 kg
- The average of fat mass in the Placebo group was 28.6 kg

Women in the ID-alG™ group had the highest fat mass (+7.7kg compared to the Placebo group).

Table 19: Fat mass between D0 & D56 / Sub-group BMI<30

Product	D0	D28	D56
Placebo	28.66	28.76	29.6
ID-alG™	36.38	33.8	33.05



Graph 7: Fat Mass variation in the Sub-group BMI < 30

At D56, the difference between the effects of both products increased, and became significant (p-value ID-alG™ vs placebo with equal variances = 0.0378).

Table 19bis: Body Fat Mass variations between D28-D0 & D56-D0 /sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.10 ± 0.43	0.1276	**0.94 ± 0.36**	**0.0378**
ID-alG™	**-2.58 ± 1.67**		**-3.32 ± 1.84**	

Variation of the body fat mass index (BFI)

The body fat index expressed in percentage consists of the proportion of fat mass on the body composition.
Some experts consider the body fat mass index as the best indicator of the fitness level, as it is the only body measurement which directly calculates the body composition without regard to the individual's height or weight.

The body fat mass index of women is greater than the one of men, due to the specific needs to cover during childbearing and other hormonal functions.

The Body Fat index (BFI) is calculated according to the formula developed by Deurenberg P *et al* (1991).*
It depends on the BMI, the sex and the age of the subjects.

In adults: **BFI = 1.20 x BMI + 0.23 x age - 10.8 x sex - 5.4**
(sex = 0 for women, and 1 for men)

Women BFI categories are

- If BFI > 30, the fat mass is considered as too important and weight loss is recommended.
- If BFI is between 25 and 30; it is considered as normal.
- And if BFI <25%, the women is considered too lean.

After 28 days of treatment, the average BFI tended to increase in the Placebo group, whereas it tended to slightly decrease in the ID-alG™ group.
The difference between ID-alG™ and Placebo was at the limit of significance.

At D56, the difference between ID-alG™ and Placebo increased and became significant.

Table 20: BFI variations between D28-D0 & D56-D0 /sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.38 ± 0.22	**0.0900**	**0.41 ± 0.20**	**0.0376**
ID-alG™	**-0.27 ± 0.25**		**-1.04 ± 0.61**	

3.4. VARIATIONS OF THE BODY LEAN MASS & BODY WATER MASS

Variation of the body lean mass

In both groups, the value of body lean mass remained constant.
No significant variation was observed in the Placebo group or in the ID-alG™ group.

Table 21: Body lean mass variations between D28-D0 & D56-D0 /sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.76 ± 0.29	0.4864	0.02 ± 0.26	0.7389
ID-alG™	1.95 ± 1.49		0.55 ± 1.43	

Variation of the body water mass

In both groups, the value of body water mass remained stable.
No significant variation was observed in the Placebo group or in the ID-alG™ group.

Table 22: Body water mass variations between D28-D0 & D56-D0 /sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	0.56 ± 0.21	0.5031	0.02 ± 0.19	0.7607
ID-alG™	1.40 ± 1.10		0.38 ± 1.05	

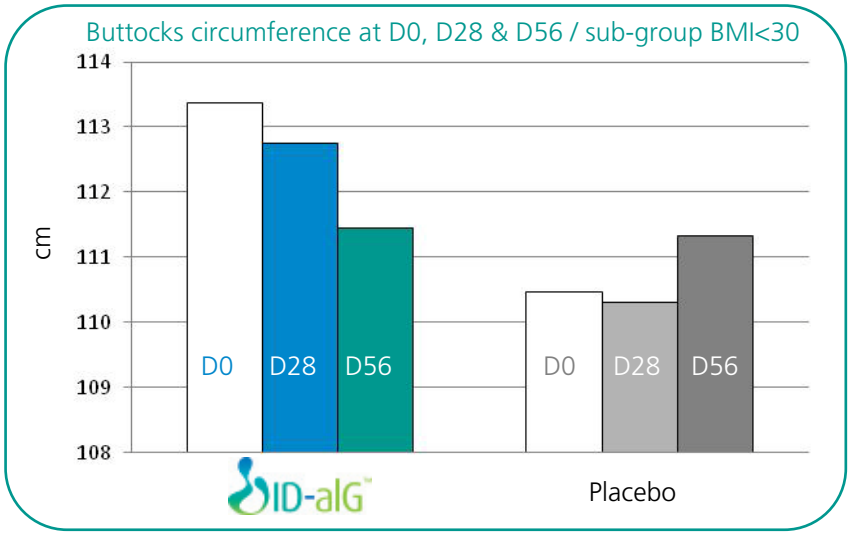
3.5. VARIATIONS OF THE CIRCUMFERENCES

- Buttocks circumference

Table 23: Buttocks circumference variations between D28-D0 & D56-D0 /sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	-0.16 ± 0.54	0.5641	**0.86 ± 0.35**	0.1496
ID-alG™	-0.63 ± 0.53		**-1.93 ± 1.45**	

After 56 days of treatment, the buttocks circumference of women in the ID-alG™ group decreased whereas the buttocks circumference of women in the Placebo group increased No significant variation was observed in between the groups.



Graph 8: Buttocks circumference at D0, D28 & D56 /sub-group BMI<30

- Hips circumference

Table 24: Hips circumference variations between D28-D0 & D56-D0 /sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	1.22 ± 0.41	0.0370	**1.76 ± 0.55**	0.4658
ID-alG™	-0.15 ± 0.30		0.88 ± 1.10	

After 56 days of treatment, hips circumference slightly increased in the Placebo group while no significant variation was observed in the ID-alG™ group.
No significant variation was observed between the groups.

- Thighs circumference

Table 25: Thighs circumference variations between D0-D28 & D0-D56 /sub-group BMI<30

Product	D28-D0	p-value inter-group	D56-D0	p-value inter-group
Placebo	-0.54 ± 0.19	0.4808	**-0.59 ± 0.22**	0.1405
ID-alG™	-0.92 ± 0.54		-1.97 ± 0.90	

After 56 days of treatment, thighs circumference slightly decreased in both groups No significant difference was observed between Placebo and ID-alG™.

3.6. VARIATIONS OF THE LIFE STYLE

Every week, volunteers filled in questionnaire to evaluate their consumption habits (type of meals and place …).

One question concerned the frequency of meals taken outside (ex: restaurants, fast-food, invitation...). This question is particularly interesting because it is usually more difficult to control the caloric value of meals taken outside.

Product	D28-D0		D56-D28	
	Outside meals frequency	Body weight variation	Outside meals frequency	Body weight variation
Placebo	0.63	0.86 kg	0.51	0.1 kg
ID-alG™	**1.07**	**-0.65 kg**	**0.73**	**-2.15 kg**

Women in the ID-alG™ group took their meals outside more often than women in the Placebo group, both during the first period (D0-D28) and the second period (D28-D56).
In this sub-group, the higher frequency of outside meals is associated with a significant weight loss. This unusual result could be linked to the weight-management effect of ID-alG™.

Conclusion on the sub-group with BMI < 30

In this sub-group (BMI < 30), women treated with ID-alG™ lost weight after 28 days according to a significant trend. This trend is confirmed one month later, with an average weight loss of 2.80 kg in the ID-alG™ group (p=0.047).
In the same period, women in the Placebo group gained weight (+0.96 kg at D56).

Variations observed on weight had an impact on BMI: BMI of women in the ID-alG™ group decreased, while the one of women in the Placebo group did not change.

Moreover, it is interesting to note that the weight loss observed in the ID-alG™ group seemed to be entirely due to a fat mass reduction (2.8kg of weight loss and 3.3kg of body fat reduction observed between D0 and D56 in the ID-alG™ group).
Variation of the body fat mass was indeed significantly different between the two groups (p =0.0378) and this trend was reinforced by the significant difference on the body fat index (BFI) (p = 0.09 at D28 and p=0.03 at D56).

When a subject loses weight, there is a risk to observe a decrease of the lean mass.
In both groups, the body lean mass and body water mass remained unchanged.

Regarding circumference measurements, buttocks and thighs decreased according to a significant trend after 56 days in the ID-alG™ group while they tended to slighly increase in the Placebo group.

4. Conclusion

This is the first clinical study designed to evaluate the weight management properties of ID-alG™ (a brown seaweed extract) on human
The preliminary results on rats were already very positive: they highlighted that ID-alG™ was able to reduce the negative effect of a hypercaloric diet on body weight and body fat gain.

This clinical study was designed to confirm these results on human. Being a first clinical study, the inclusion critera allowed a wide range of BMI: from 28 to 39.

This large inclusion was both an advantage and a disadvantage:

- On one side it was difficult to show significant results on the *Per Protocol* population, because of a great heterogeneity of the population.
- On the other side, this large range of BMI allowed making a statistical analysis according to the BMI class and we clearly observed that ID-alG™ was particularly adapted to overweight persons. ID-alG™ helps to reduce body weight and body fat mass, and improve figures on women with BMI < 30.

As a conclusion, we can say that this study was successful and allows to confirm the full range of weight-management properties of ID-alG™: weight-control, reduction of fat storage/ body fat mass, caloric intake control without frustration nor lifestyle modification…
Moreover, no side effect and no adverse event were reported, which represents an essential advantage for ID-alG™ as an efficient weight-management ingredient.

This study goes deep into details. The food questionnaire should reveal other precious information, for example: a potential effect of ID-alG™ on the diet and behavior…
Additional analyses are needed and will soon be available….

SUMMARY OF RESULTS (average values after 56 days)

		Per protocol Population		**Sub-group BMI<30**	
		Placebo	**ID-alG™**	Placebo	**ID-alG™**
Body composition/ body weight	Fat mass variation	0.12 kg	-0.25 kg	**0.94 kg**	**-3.32 kg**
	BMI variation	-0.02	-0.09	**0.34**	**-0.90**
	Body weight variation	0.02kg	-0.22 kg	**0.96 kg**	**-2.80 kg**
Anthropometrical parameters	Buttocks	0.48 cm	-0.26 cm	0.86 cm	-1.93 cm
	Thighs	-1.00 cm	-1.06 cm	-0.59 cm	-1.97 cm