BACKGROUND AND AIMS
Over 1 billion people worldwide live with prediabetes, which is defined by increased fasting blood glucose (FBG), glucose intolerance and/or higher A1c hemoglobin. Prediabetes is considered a risk factor for Type 2 Diabetes (T2D).

TOTUM-63 is a plant-based product designed to reduce T2D risk factors. TOTUM-63 has been demonstrated to significantly improve body weight and glucose homeostasis in animal models of obesity and type 2 diabetes (db/db and C57BL/6 fed a high-fat diet). In a Phase I/II clinical trial, TOTUM-63 had shown its safety, good tolerance and beneficial effects on post-prandial glucose control in individuals living with overweight.

The aim of this multicenter, randomized and double-blind placebo-controlled Phase II trial was to assess the effects of TOTUM-63 on glucose homeostasis in individuals with impaired fasting glycemia and glucose intolerance.

MATERIALS AND METHODS

Study design
• Multicenter, randomized, unbalanced (3:1, TOTUM-63:Placebo) and double-blind placebo-controlled study, 2 parallel-groups.
• Supplementation period: 6 months, 5 g/day (3 intakes).
• Primary endpoint: change in fasting glycemia between baseline and 6 months.
• Main secondary endpoints: 2-hour OGTT glycemia, insulin sensitivity, anthropometric parameters, hemodynamic parameters, lipid profile, safety.

Main inclusion criteria
• Age between 35 and 75 years (limits included).
• Waist circumference > 94 cm for men or > 80 cm for women.
• Fasting glycemia > 6.1 mmol/L (1.1 g/L).
• 2-hour glycemia (OGTT) > 7.8 mmol/L (1.4 g/L).
• HbA1c < 8.6 mmol/L.
• Age between 35 and 75 years (limits included).
• Body weight change < 5% in the 3 months prior the randomization.
• With reported body weight variation < 5% in the 3 months before randomization and agreeing to keep them unchanged throughout the study (no hyper-hypocaloric diet nor start-stop of sport activity planned in the next 7 months).

Safety outcomes
- 10 adverse events whose relationship with the study’s product were not excluded, were gastrointestinal disorders (abdominal pain, diarrhea or nausea).

RESULTS

Study population at baseline
• Age*: 57.1 years (± 1.4)
• Gender: 35 female, 16 male
• BMI*: 31.3 kg/m² (± 0.8)
• Fasting glycemia*: 6.93 mmol/L (± 0.17)
• 2-hour OGTT glycemia*: 10.25 mmol/L (± 0.42)
• HbA1c*: 6.98 mmol/L (± 0.11)
• Fasting triglycerides*: 1.99 mmol/L (± 0.13)

Here are the characteristics of the study population at baseline. No statistical difference was evidenced between groups at baseline.

Main inclusions criteria expressed in %)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline</th>
<th>6 months</th>
<th>Change</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>31.3 kg/m²</td>
<td>30.7 kg/m²</td>
<td>-0.6 kg/m²</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>94 cm</td>
<td>90 cm</td>
<td>-4 cm</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.99 mmol/L</td>
<td>1.89 mmol/L</td>
<td>-0.1 mmol/L</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Primary endpoint reached: reduction in fasting glycemia vs. placebo, from baseline to 6 months.

TOTUM-63 LOWERS FASTING GLYCEMIA IN SUBJECTS WITH PREDIABETES: A PHASE II CLINICAL TRIAL

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CONCLUSION
• TOTUM-63 was very well tolerated and no change was observed in safety parameters (blood cell count, renal function, hepatic function).
• At the end of the supplementation period, FBG (primary endpoint) was reduced in TOTUM-63 group compared to placebo group (placebo-corrected difference from baseline: -9.3%, p<0.05).
• Similarly, 2-hour OGTT glycemia was improved in TOTUM-63 group, vs. placebo (placebo-corrected difference from pre-protocol value: -22.5%, p<0.05).
• Moreover, TOTUM-63 had a significant lowering effect on body weight (placebo-corrected difference from baseline: -1.9 Kg, p<0.05) and waist circumference (-4.5 cm, p<0.001).
• Furthermore, TOTUM-63 also improved lipid profile and reduced systolic blood pressure.

This randomized and double-blind placebo-controlled Phase II trial showed that TOTUM-63 contributed to lower fasting blood glucose in individuals with impaired fasting glycemia and glucose intolerance. Moreover, TOTUM-63 also improved many metabolic and anthropometric parameters often impaired in individuals living with prediabetes and T2D. This study opens the door to larger trials and makes TOTUM-63 a promising candidate for T2D risk prevention.

No statistically significant difference between groups on the proportion of subjects with:
- Serious AEs.
- Moderate or severe AEs.
- AEs in relationship with research.
- AEs in relationship with the study’s product.

Disclosure: Sébastien PELTIER is CEO of VALBIOTIS. Vivien CHAVANELLE, Yolanda OTERO, Maxime BARGETTO, Murielle CAZAUBIEL and Pascal SIRVENT are employed by VALBIOTIS.