

Baseline of the REVERSE-IT study – a 24-week and 600-people randomised placebo-controlled study of the metabolic effects of TOTUM•63 (T63), a five plant-extract combination

Y. F. Otero¹, P. Sirvent¹, OE Johansen², V. Chavanelle¹, M. Bargetto¹, V. Sapone¹, A. Bouchard-Mercier¹, F. Le Joubioux¹, N. Boisseau³, T. Maugard⁴, M. Cazaubiel¹, B. Pereira⁵, B. Guigas⁶, S. Hadjadj⁷, S. Peltier¹, A. Marette⁸, J.M. Bard⁹

¹Valbiotis, France; ²Nestlé Health Science, Switzerland; ³Clermont Auvergne University, France; ⁴La Rochelle University, France; ⁵CHU Clermont-Ferrand, France; ⁶Leiden University, Netherlands; ⁷CHU Nantes, France; ⁸Laval University, Canada; ⁹Nantes University, France

BACKGROUND

- The role of natural based products to support glucose control in people with prediabetes or early type 2 diabetes (T2D) is debated¹, partly related to lack of robust clinical evidence.
- T63 is a polyphenol-rich substance composed by artichoke, chrysanthellum, olive leaf, bilberry, and black pepper extracts that previously demonstrated metabolic beneficial effects in preclinical studies²⁻⁴ as well as in a phase IIa clinical study⁵.
- T63 is now being studied in the large pivotal REVERSE-IT study.

METHODS

- REVERSE-IT (NCT04423302) is a 24 weeks, multicentre, multi-country clinical trial involving people with dysglycemia.
- Key inclusion criteria:
 - Age 18 - 70 years;
 - Prediabetes or newly diagnosed type 2 diabetes;
 - BMI 25 - 40 kg/m²;
 - Waist circumference > 102 cm for men and > 88 cm for women.
- Key exclusion criteria:
 - Use of glucose lowering medication (e.g., biguanides, sulfonylureas, glinides, gliptines, glitazones, gliflozines, α-glucosidase inhibitors, incretins and insulin);
 - Newly introduced, or dose-changes of lipid-lowering treatment (e.g. statins, fibrates, ezetimibe, bile acid sequestrants, niacin, etc.), 3 months prior randomization.
- The study tests the hypothesis that 5g of T63 vs. placebo (PBO) leads to a significant reduction in fasting plasma glucose.
- Secondary outcomes include effects on HbA1c, lipids, blood pressure, weight, waist circumference, and C-reactive protein.
 - Effects on 2-point OGTT will be assessed in a substudy.
- The primary analysis will compare T63 vs. PBO when provided thrice a day (TID double-blinded fashion), while an open label analysis will compare effects of T63 vs. PBO provided twice a day (BID).
- Comprehensive clinical evaluations are conducted at baseline, 12 weeks and 24 weeks (Figure).

Figure. REVERSE-IT study design

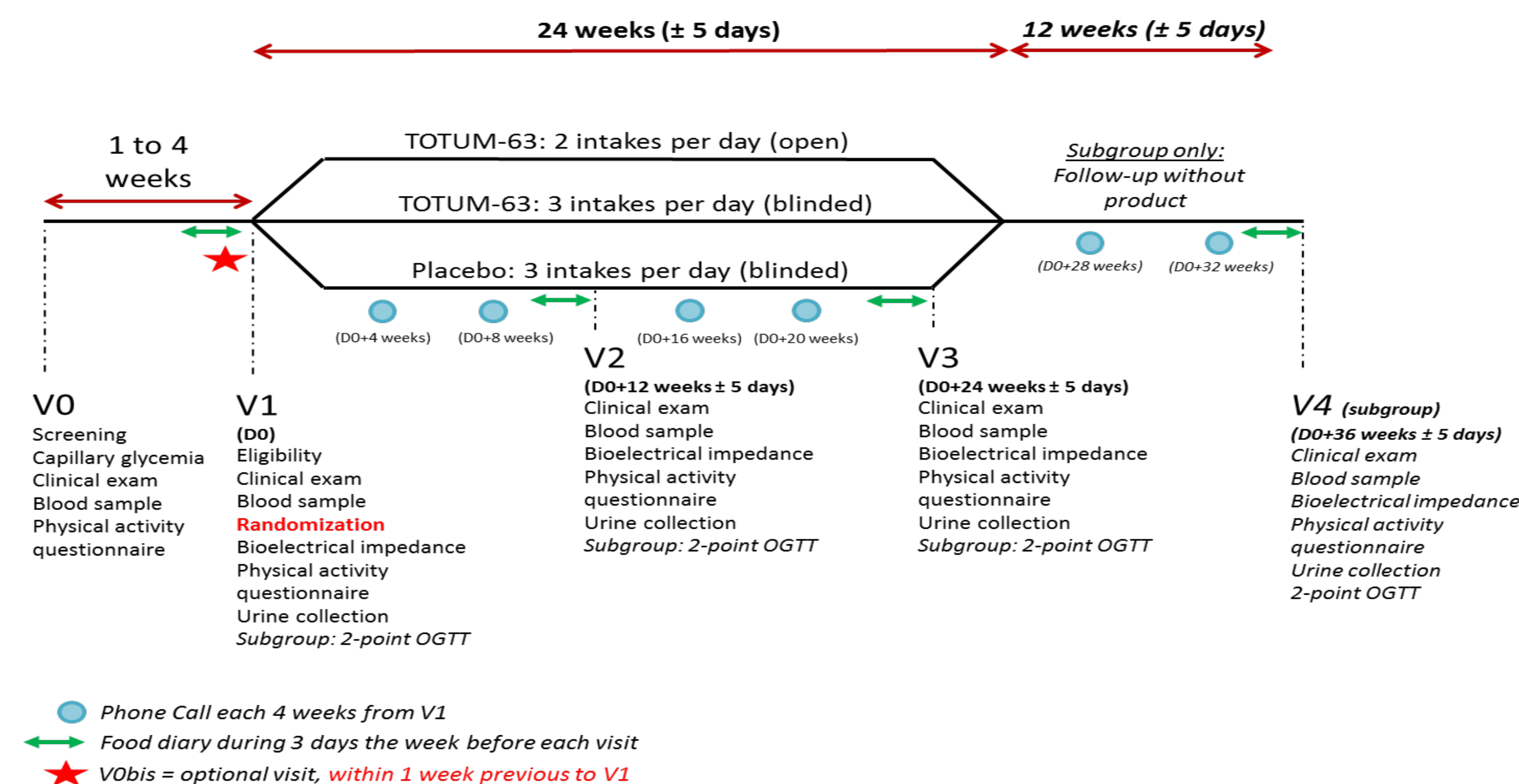


Table. Baseline characteristics of participants in the REVERSE-IT study overall and by glycemia category. Data are n (%) or mean (standard deviation).

	Total population		Prediabetes		Type 2 diabetes	
	Mean / n	SD / %	Mean / n	SD / %	Mean / n	SD / %
N (%)	636 (100%)		501 (78.8)		135 (21.2)	
Females	372	59.3	298	60.7	74	54.4
Males	264	42.1	203	41.3	61	44.9
Age (years)	56.5	9.1	56.4	9.2	57.0	8.4
Country participants						
France	141	22.2	122	24.4	19	14.1
Germany	163	25.6	122	24.4	41	30.4
Italy	43	6.8	34	6.8	9	6.7
Poland	14	2.2	12	2.4	2	1.5
Romania	80	12.6	53	10.6	27	20.0
Bulgaria	140	22.0	120	24.0	20	14.8
Hungary	55	8.6	38	7.6	17	12.6
Anthropometrics and clinical characteristics						
Weight (kg)	92.4	16.4	91.7	16.1	94.8	17
BMI (kg/m ²)	31.7	4.8	31.6	4.6	32.7	5.4
Waist circumference (cm)	109.1	12.5	108.6	12.4	111	13
HbA1c (%)	6.11	0.85	5.90	0.54	6.89	1.24
HbA1c (mmol/mol)	43	6	41	4	52	9
Fasting plasma glucose (mg/dl)	123	22	116	14	146	30
eGFR (mL/min/1.73 m ²)	87.6	13.9	87.6	14.0	87.6	13.3
Total cholesterol (mmol/L)	4.93	1.08	4.95	1.06	4.85	1.13
LDL cholesterol (mmol/L)	2.99	0.94	3.01	0.93	2.9	0.96
HDL cholesterol (mmol/L)	1.27	0.34	1.29	0.35	1.2	0.3
Triglycerides (mmol/L)	1.52	0.83	1.47	0.84	1.64	0.79
Systolic blood pressure (mmHg)	133	12	132	12	135	11
Diastolic blood pressure (mmHg)	81	8	81	8	82	8
Heart rate (bpm)	72	9	72	9	73	9

RESULTS

- A total of 636 people were recruited over 2 years from 61 centers across 7 European countries (France, Germany, Italy, Bulgaria, Hungary, Poland and Romania).
- Mean age is 56.5±9 years, BMI 31.7±4.8 kg/m² and HbA1c 6.11±0.85% (Table).
- Most of the participants have prediabetes (78.8%), who appear to have a better glucometabolic profile compared to people with type 2 diabetes (21.2% of the population);
 - Fasting plasma glucose: 116±14 mg/dl vs 146±30 mg/dl;
 - Systolic BP 132±12 mmHg vs 135±11 mmHg;
 - BMI 31.6 kg/m² vs 32.7 kg/m².

CONCLUSION

- REVERSE-IT has enrolled an appropriate population to help inform clinical decision making on the use of plant-extract based TOTUM•63 to support glucose homeostasis in people with prediabetes and type 2 diabetes.
- The size of the study, and its multi-country and multicenter involvement, will provide reassurance on generalizability of results.
- Readout is expected second half of 2023.
- Comprehensive scientific presentation of results is expected first half of 2024

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DISCLOSURES

T63 is a patented formulation developed by Valbiotis and licensed to Nestlé Health Science. YFO, PS, VC, ABM, FLJ, MC, SP are employees of Valbiotis. OEJ is employed by Nestlé Health Science, a license partner of Valbiotis. NB, TM, BP, BG, SH, AM and JMB are members of the Valbiotis scientific and medical board.