

Supplementary material to:

Clinical features, cardiovascular risk profile, and therapeutic trajectories of patients with type 2 diabetes candidate for oral semaglutide therapy in the Italian specialist care

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Figure S1. Patients selection and flow-chart.

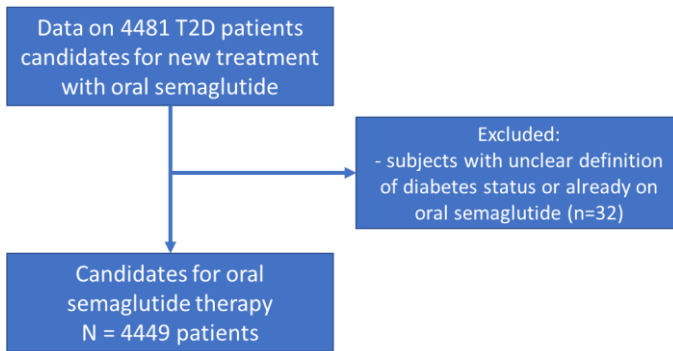


Figure S2. Heatmap showing the relationship between main clinical characteristics and reason to choose oral semaglutide as treatment. Note: scale is the log(OR) for the association between each factor and different reasons. Red colors depicted a positive log(OR) meaning that clinical characteristics were associated with higher relevance of specific reason. Cells with * shows significant association with $p < 0.05$, ** $p < 0.0005$.

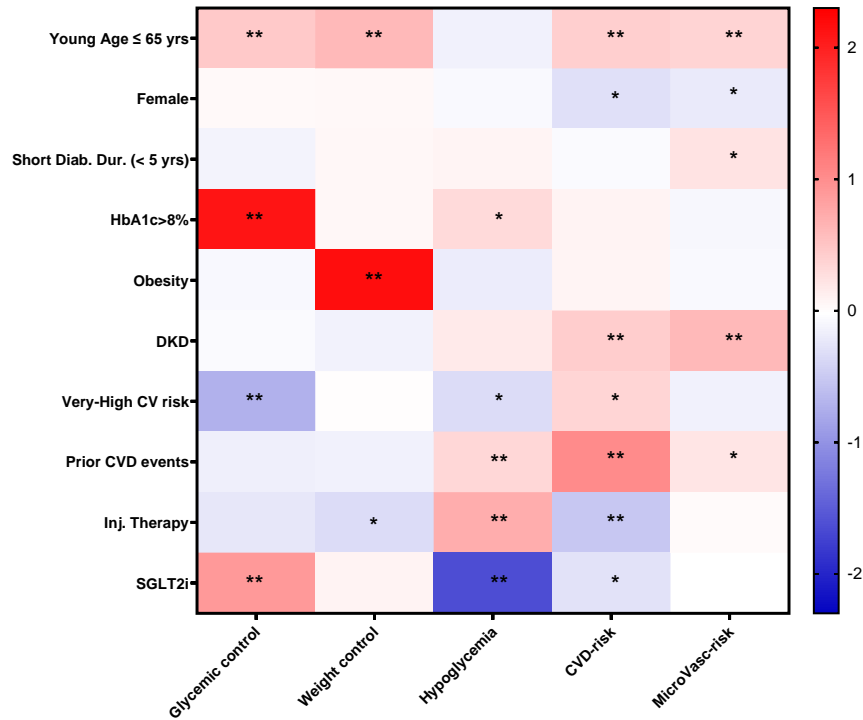


Table S1. Expected HbA1c reduction after add-on of oral semaglutide according to background regimen. Mean changes from semaglutide 14 mg or (flexible dosing) vs PLB in each trial was used as reference for expected HbA1c reduction, when PLB arm was not present then the pre-post treatment was used as reference for expected HbA1c reduction adding 0,2% (that is the median changes in PLB groups observed in similar studies, e.g. from - 1.3% observed as pre-post to -1.1% used as expected reduction).

Condition 1 (change in treatments)	Condition 2 (Background therapy)	Expected response on Hba1c %	Expected response similar to:
IF	AND No treatment	- 1.1	Pioneer 1
ELSE IF	AND Metformin alone	- 1.1	Pioneer 2
ELSE IF	AND Metformin + SU	- 1.1	Pioneer 3
ELSE IF	AND Metformin + SGLT2i	- 1.0	Pioneer 4
ELSE IF	AND Metformin + Insulin	- 1.0	Pioneer 8
ELSE IF	AND Mono or dual therapy	- 1.1	Pioneer 7
ELSE IF	AND DKD	- 0.8	Pioneer 5
ELSE		- 0.7	Pioneer 6

Table S2. Characteristics of patients according to specific subgroups of background regimen. Continuous variables are presented as mean \pm standard deviation, while categorical variables are presented as number (%).

Characteristics	Available	Total	Naive	Only Metformin	Metformin + DPP4i	Metformin + SGLT2i	Metformin + SU	Metformin + Insulin
No of Subjects		4449	425 (10%)	1380 (31%)	626 (14%)	528 (12%)	278 (6%)	276 (6%)
Female	99%	1736 (39.6%)	179 (42.5%)	556 (41.1%)	254 (41.5%)	166 (31.8%)	105 (38.3%)	98 (35.9%)
Age, years	96%	63.4 \pm 10.1	56.9 \pm 10.4	61.6 \pm 10.1	65.2 \pm 9.1	64.3 \pm 9.2	67.4 \pm 9.3	65.3 \pm 9.8
Diabetes Duration < 5 yrs	100%	1853 (41.8%)	385 (90.8%)	778 (56.5%)	198 (31.7%)	149 (28.3%)	72 (25.9%)	63 (22.8%)
Diabetes Duration 5-10 yrs	100%	1381 (31.1%)	22 (5.2%)	387 (28.1%)	250 (40.0%)	213 (40.4%)	105 (37.8%)	73 (26.4%)
Diabetes Duration > 10 yrs	100%	1204 (27.1%)	17 (4.0%)	211 (15.3%)	177 (28.3%)	165 (31.3%)	101 (36.3%)	140 (50.7%)
Active smoker	99%	1194 (27.1%)	141 (33.3%)	343 (25.4%)	204 (32.7%)	148 (28.2%)	77 (28.0%)	58 (21.2%)
Good/optimal Diet	93%	1069 (25.8%)	141 (35.6%)	299 (23.2%)	143 (25.4%)	110 (22.4%)	81 (30.0%)	66 (24.5%)
Regular physical activity	98%	608 (13.9%)	79 (18.9%)	225 (16.5%)	69 (11.2%)	57 (10.8%)	32 (11.8%)	47 (17.4%)
Latest HbA1c, %	96%	7.9 \pm 1.1	8.2 \pm 1.5	7.9 \pm 1.2	7.9 \pm 0.9	7.9 \pm 0.8	8.0 \pm 1.0	8.2 \pm 1.3
HbA1c personalize target, %	82%	6.8 \pm 0.3	6.6 \pm 0.4	6.7 \pm 0.3	6.8 \pm 0.3	6.7 \pm 0.3	6.9 \pm 0.3	6.9 \pm 0.4
HbA1c Distance to target, %	82%	1.2 \pm 1.1	1.6 \pm 1.5	1.2 \pm 1.2	1.0 \pm 0.9	1.0 \pm 0.8	1.1 \pm 1.0	1.3 \pm 1.2
Body mass index, kg/m ²	92%	30.6 \pm 5.2	31.8 \pm 5.5	30.9 \pm 5.2	30.1 \pm 4.5	30.7 \pm 5.9	30.2 \pm 4.6	30.0 \pm 5.5
Obesity	92%	2078 (50.5%)	257 (62.1%)	639 (51.8%)	269 (50.0%)	232 (47.8%)	133 (48.7%)	123 (46.1%)
Hypertension	100%	3387 (76.1%)	267 (62.8%)	959 (69.5%)	505 (80.7%)	448 (84.8%)	223 (80.2%)	225 (81.5%)
Dyslipidaemia	100%	2915 (65.5%)	223 (52.5%)	901 (65.3%)	406 (64.9%)	372 (70.5%)	194 (69.8%)	189 (68.5%)
LDL-Cholesterol, mg/dl	80%	97.5 \pm 37.0	107.4 \pm 38.7	101.0 \pm 36.6	98.5 \pm 33.6	90.7 \pm 38.8	97.0 \pm 37.4	93.2 \pm 43.0
Non-HDL Cholesterol, mg/dl	81%	128.6 \pm 40.8	142.4 \pm 47.9	132.5 \pm 40.7	129.2 \pm 37.8	122.3 \pm 41.9	128.5 \pm 39.4	122.9 \pm 39.4
Renal disease	100%	1466 (33.0%)	81 (19.1%)	284 (20.6%)	213 (34.0%)	217 (41.1%)	106 (38.1%)	114 (41.3%)
eGFR (CKD-epi) ml/mi/1.73 m ²	85%	79.2 \pm 19.9	84.1 \pm 20.7	83.4 \pm 17.9	76.0 \pm 18.2	80.0 \pm 18.9	76.2 \pm 18.9	78.2 \pm 20.2
CKD III stage	85%	683 (18.1%)	36 (10.2%)	107 (9.4%)	93 (19.5%)	86 (18.9%)	53 (21.4%)	54 (20.5%)
Micro-albuminuria	92%	989 (24.2%)	54 (13.8%)	189 (15.2%)	143 (24.6%)	155 (31.6%)	71 (27.4%)	83 (32.3%)
Macro-albuminuria	92%	92 (2.2%)	8 (2.1%)	10 (0.8%)	12 (2.1%)	10 (2.0%)	9 (3.5%)	9 (3.5%)
CVD risk assessments								
Very High risk	100%	1494 (33.6%)	112 (26.4%)	374 (27.1%)	174 (27.8%)	225 (42.6%)	101 (36.3%)	125 (45.3%)
High risk	100%	2703 (60.8%)	270 (63.5%)	861 (62.4%)	428 (68.4%)	293 (55.5%)	168 (60.4%)	145 (52.5%)
Moderate risk	100%	252 (5.7%)	43 (10.1%)	145 (10.5%)	24 (3.8%)	10 (1.9%)	9 (3.2%)	6 (2.2%)
No with CVRF \geq 3	100%	822 (18.5%)	67 (15.8%)	234 (17.0%)	96 (15.3%)	128 (24.2%)	55 (19.8%)	51 (18.5%)
Complications								
Prior CVD events	100%	695 (15.6%)	56 (13.2%)	156 (11.3%)	70 (11.2%)	106 (20.1%)	46 (16.5%)	73 (26.4%)
Stroke	100%	147 (3.3%)	12 (2.8%)	23 (1.7%)	18 (2.9%)	12 (2.3%)	11 (4.0%)	15 (5.4%)
Myocardial infarction	100%	466 (10.5%)	41 (9.6%)	105 (7.6%)	43 (6.9%)	78 (14.8%)	36 (12.9%)	54 (19.6%)
Angina	100%	68 (1.5%)	4 (0.9%)	23 (1.7%)	8 (1.3%)	8 (1.5%)	2 (0.7%)	4 (1.4%)

PAD	100%	82 (1.8%)	4 (0.9%)	20 (1.4%)	6 (1.0%)	11 (2.1%)	5 (1.8%)	10 (3.6%)
Organ Damage	100%	356 (8.0%)	20 (4.7%)	64 (4.6%)	45 (7.2%)	66 (12.5%)	29 (10.4%)	28 (10.1%)
Heart Failure	100%	302 (6.8%)	13 (3.1%)	31 (2.2%)	35 (5.6%)	56 (10.6%)	16 (5.8%)	24 (8.7%)