SUPPLEMENTARY MATERIAL

Table S1. Change in total daily insulin dose and type of insulin administration

MDI	All (n=134)	Baseline HbA1c <7.0% [53 mmol/mol] (n=7)	Baseline HbA1c 7.0-8.0% [53-64 mmol/mol] (n=55)	Baseline HbA1c >8.0% [64 mmol/mol] (n=72)	Baseline BMI ≤27, kg/m2 (n=37)	Baseline BMI >27, kg/m2 (n=97)
Basal TDI at baseline, IU/Kg	0.395 ±0.17	0.408 ±0.15	0.377 ±0.14	0.408 ±0.19	0.402 ±0.19	0.393 ±0.16
Basal TDI at 12 months, IU/Kg	0.347 ±0.14 (p=0.000)	0.399 ±0.15 (p=0.764)	0.320 ±0.12 (p=0.000)	0.363 ±0.16 (p=0.000)	0.354 ±0.17 (p=0.000)	0.344 ±0.13 (p=0.000)
Basal TDI difference at 12 months (%)	-0.048 (-12.2%)	-0.009 (-2.2%)	-0.057 (-15.1%)	-0.045 (-11.0%)	-0.048 (-11.9%)	-0.049 (-12.5%)
Prandial TDI at baseline, IU/Kg	0.325 ±0.17	0.287 ±0.17	0.308 ±0.14	0.341 ±0.19	0.293 ±0.11	0.336 ±0.19
Prandial TDI at 12 months, IU/Kg	0.301 ±0.14 (p=0.004)	0.276 ±0.15 (p=0.518)	0.279 ±0.12 (p=0.004)	0.318 ±0.16 (p=0.087)	0.285 ±0.11 (p=0.433)	0.305 ±0.15 (p=0.005)
Prandial TDI difference at 12 months (%)	-0.024 (-7.4%)	-0.011 (-3.8%)	-0.029 (-9.4%)	-0.023 (-6.7%)	-0.008 (-2.7%)	-0.031 (-9.2%)
CSII	All (n=65)	Baseline HbA1c <7.0% [53 mmol/mol] (n=3)	Baseline HbA1c 7.0-8.0% [53-64 mmol/mol] (n=24)	Baseline HbA1c >8.0% [64 mmol/mol] (n=38)	Baseline BMI ≤27, kg/m2 (n=26)	Baseline BMI >27, kg/m2 (n=39)
TDI at baseline, IU/Kg	0.525 ±0.18	0.410 ±0.04	0.530 ±0.22	0.531 ±0.14	0.517 ±0.16	0.532 ±0.20
TDI at 12 months, IU/Kg	0.487 ±0.14 (p=0.035)	0.315 ±0.05 (p=0.033)	0.463 ±0.14 (p=0.024)	0.523 ±0.13 (p=0.748)	0.466 ±0.15 (p=0.003)	0.506 ±0.14 (p=0.389)
TDI difference at 12 months (%)	-0.038 (-7.2%)	-0.095 (-23.2%)	-0.067 (-12.6%)	-0.008 (-1.5%)	-0.051 (-9.9%)	-0.026 (-4.9%)

CSII: continuous subcutaneous insulin infusion; MDI: multiple daily injections; TDI: total daily insulin dose.

Table S2. Changes in eGFR and microalbuminuria status from baseline to 12 months

	At baseline (n=142)	At 12 months (n=142)	Progression/Regression n (%)
eGFR ≥ 90 ml/min/1.73m^2	95 (66.9%)	105 (73.9%)	+10 (+10.5%)
eGFR < 90 ml/min/1.73m^2	47 (33.1%)	37 (26.1%)	-10 (-21.3%)
	At baseline (n=134)	At 12 months (n=134)	Progression/Regression n (%)
UACR <15 mg/g	120 (89.6%)	122 (91.0%)	+2 (+1.7%)
UACR ≥15 mg/g	14 (10.4%)	12 (9.0%)	-2 (-14.2%)

eGFR: estimated glomerular filtration rate; UACR: urinary albumin-to-creatinine ratio.

Table S3. Genital infection and diabetic ketoacidosis according to SGLT2 inhibitor type and dose*

	Empa-gliflozin 5mg (n=50)	Empa-gliflozin 10mg (n=47)	Empa-gliflozin 12.5mg (n=9)	Empa-gliflozin 25mg (n=7)	Dapagli-flozin 5mg (n=26)	Dapagli-flozin 10mg (n=41)	Cana-gliflozin 50mg (n=1)	Cana-gliflozin 100mg (n=18)
Genital infection (n=45)	9 (18%)	11 (23.4%)	3 (33.3%)	1 (14.3%)	10 (38.5%)	9 (22.0%)	0 (0.0%)	2 (11.1%)
DKA (n=7)	2 (4.0%)	2 (4.3%)	1 (11.1%)	1 (14.3%)	0 (0.0%)	1 (2.4%)	0 (0.0%)	0 (0.0%)

DKA: Diabetic ketoacidosis; *The SGLT2i (type and dose) registered corresponded to the one the patient was receiving at the time of the adverse event.

Table S4. Differences on adverse events between Belgium and Spain

All (n=199)	Belgium (n=71)	Spain (n=128)
Any adverse event* (n=57)	25 (35.2%)	32 (25.0%)
2 adverse events* (n=1)	1 (1.4%)	0 (0.0%)
Genital infection (n=45)	20 (28.2%)	25 (19.5%)
Ketosis (n=5)	2 (2.8%)	3 (2.3%)
Diabetic ketoacidosis (n=7)	3 (4.2%)	4 (3.1%)
Severe hypoglycemia (n=0)	0 (0.0%)	0 (0.0%)
Adverse events leading to discontinuation of treatment (n= 15)	8 (11.3%)	7 (5.5%)

Table S5. Change from baseline in HbA1c, weight, total daily insulin dose and renal function: in-label SGLT2 inhibitors prescription versus off-label

	*IN-LABEL SGLT2i (N=20)	OFF-LABEL SGLT2i (N=179)
Baseline HbA1c, % [mmol/mol] (mean, SD)	8.3 (± 0.9) [67.2]	8,2 (± 0.9) [66.1]
12m HbA1c, % [mmol/mol] (mean, SD)	7.6 (± 0.7) [59.6]	7.7 (± 0.7) [60.7]
HbA1c difference	-0.7 (p= 0.004)	-0.5 (p< 0.001)
Baseline weight, kg (mean, SD)	90.3 (± 10.2)	82.8 (± 15.0)
12m weight, kg (mean, SD)	85.8 (±11.8)	80.0 (± 15.2)
Weight difference	-4.5 (p= 0.002)	-2.7 (p <0.001)
TDI at baseline, IU/kg (mean, SD)	0.627 (±0,26)	0.673 (±0.27)
TDI at 12m, IU/kg (mean, SD)	0.599 (±0,27)	0.606 (± 0.22)
TDI difference	-0.028 (p= 0.234)	-0.067 (p< 0.001)
Baseline eGFR, ml/min/1.73 m^2 (mean, SD)	100.1 (± 20.3)	96.8 (± 14.5)
12m eGFR, ml/min/1.73 m^2 (mean, SD)	98.1 (± 22.5)	98.4 (± 15.2)
eGFR difference	-2.0 (p= 0.414)	+1,5 (p= 0.105)
Baseline UACR, mg/g (mean, SD)	6.8 (± 6.3)	10.0 (± 16.7)
12m UACR, mg/g (mean, SD)	6.0 (± 3.0)	12.6 (± 34.3)
UACR difference	-0,8 (p= 0.550)	+2,6 (p= 0.391)

eGFR: estimated glomerular filtration rate; SGLT2i: SGLT2 inhibitor; TDI: total daily insulin dose; UACR: urinary albumin-to-creatinine ratio. *In-label SGLT2i prescription: dapagliflozin 5mg, BMI> 27kg/m2.

Table S6. Adverse events with SGLT2 inhibitors: in-label SGLT2 inhibitors prescription versus off-label

	IN-LABEL SGLT2i (N=20)	OFF-LABEL SGLT2i (N=179)
Any adverse event (n, %)	6 (30.0)	51 (28.5)
2 adverse events (n, %)	0 (0.0)	1 (0.6)
Genital infection (n, %)	6 (30.0)	39 (21.8)
Ketosis (n, %)	0 (0.0)	5 (2.8)
Diabetic ketoacidosis (n, %)	0 (0.0)	7 (3.9)
Severe hypoglycemia (n, %)	0 (0.0)	0 (0.0)
Severe polyuria (n, %)	0 (0.0)	1 (0.6)
Adverse events leading to discontinuation of treatment (n, %)	2 (10.0)	13 (7.3)

SGLT2i: SGLT2 inhibitor.

Table S7. Prescribing trends between Belgium and Spain

	Empa-gliflozin 5mg (n=50)	Empa-gliflozin 10mg (n=48)	Empa-gliflozin 12.5mg (n=8)	Empa-gliflozin 25mg (n=7)	Dapa-gliflozin 5mg (n=25)	Dapa-gliflozin 10mg (n=41)	Cana-gliflozin 50mg (n=2)	Cana-gliflozin 100mg (n=18)
Belgium (n=71)	9	15	7	5	12	21	0	2
Spain (n=128)	41	33	1	2	13	20	2	16