Characterization of Tirzepatide-Treated Patients Achieving HbA1c <5.7% in the SURPASS 1-4 Trials

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OBJECTIVE

- To characterize subsets of tirzepatide-treated type 2 diabetes (T2D) patients who achieved different HbA1c targets (<5.7%, 5.7-6.5%, or >6.5%) in the SURPASS 1-4 clinical trials.

CONCLUSION

Summary

- Patients achieving HbA1c <5.7% were noted to be slightly younger, with shorter duration of type 2 diabetes (T2D), and lower HbA1c at baseline.
- Greater reduction in HbA1c, FSG, body weight, BMI, waist circumference, BP, liver enzymes, as well as greater improvement in lipid parameters, were observed in patients achieving HbA1c <5.7%, which may be associated with a decreased risk of long-term cardiometabolic complications.

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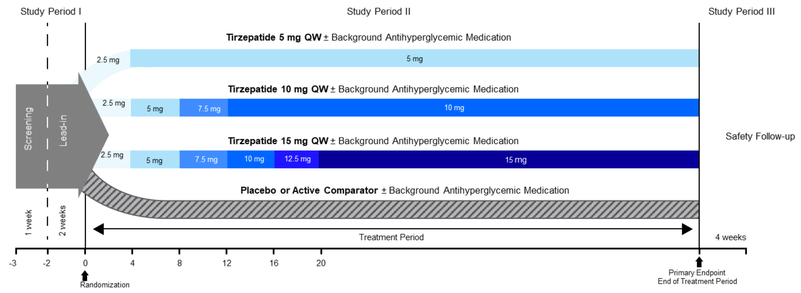
BACKGROUND

- Tirzepatide, a once weekly GIP/GLP-1 receptor agonist, recently approved in the US for treatment of people with T2D and obesity, demonstrated clinically meaningful improvements in glycemic control with 23% to 62% of patients achieving HbA1c levels below the upper normal limit (<5.7%) at the primary endpoints in addition to robust weight loss in adults with T2D in the SURPASS program.

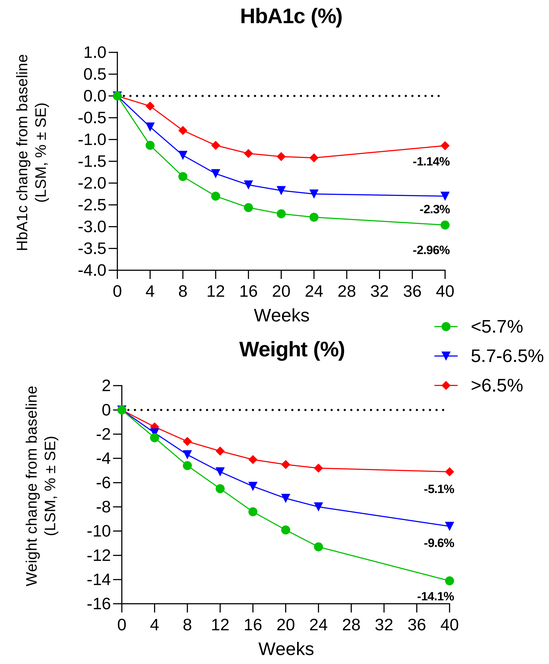
STUDY DESIGN



	Sample Size, Randomization ratio, Background glucose lowering therapy	Comparator	Primary end point
SURPASS-1	(N=478) 1:1:1:1 None	Placebo QW	Week 40
SURPASS-2	(N= 1879) 1:1:1:1 + Metformin	Semaglutide 1 mg QW	Week 40
SURPASS-3	(N=1444) 1:1:1:1 + Metformin ± SGLT-2i	Titrated Insulin Degludec QD	Week 52
SURPASS-4	(N=2002) 1:1:1:3 ± Metformin ± SU ± SGLT-2i	Titrated Insulin Glargine QD	Week 52

KEY RESULT

Greater and more rapid reductions in HbA1c and body weight were observed in patients who achieved HbA1c <5.7% at week 40



Change from baseline in HbA1c and body weight over time. LSM change in HbA1c and body weight from baseline to Week 40. Abbreviations: HbA1c=hemoglobin A1c; LSMean=least squares mean; SE=Standard Error.

Methods

- Baseline characteristics and change from baseline to Week 40 for several efficacy parameters were analyzed using descriptive statistics (mean and standard deviation for continuous variables, counts and percentages for categorical variables), for compliant patients (≥75% doses received), on treatment without rescue medication.
- Timepoint assessed = 40 weeks (SURPASS-1, -2 and -3) or 42 weeks (SURPASS-4). Waist circumference data for SURPASS-4 were not available at either Week 40 or 42, therefore Week 36 measures were used for SURPASS-4.
- The "Other" category for baseline antihyperglycemic medication refers to patients taking one oral medication that is not metformin.
- Mixed Models for Repeated Measures (MMRM) were used to model the trends for the change from baseline over time for HbA1c and percentage change from baseline over time for weight. The model terms included baseline values, study, geographical regions, HbA1c targets, visit, and HbA1c target-by-visit interaction.

Baseline demographics and clinical characteristics by HbA1c subset

HbA1c Subsets at Week 40	Patients Who Achieved <5.7% (N=1209)	Patients Who Achieved 5.7-6.5% (N=1407)	Patients Who Achieved >6.5% (N=613)
	Baseline Characteristics ± SD		
Age (y)	56 ± (10.4)	59 ± (10.1)	59 ± (10.0)
Male/Female (%)	54/46	54/46	53/47
Duration of Diabetes (y)	7.5 ± (6.18)	9.3 ± (6.91)	11.0 ± (7.50)
	Baseline Antihyperglycemic Therapy (%)		
Metformin Only	842 (69.6)	845 (60.1)	346 (56.4)
More than OAM	247 (20.4)	397 (28.2)	205 (33.4)
No OAM	112 (9.3)	143 (10.2)	48 (7.8)
Other	8 (0.7)	22 (1.6)	14 (2.3)
	Clinical Baseline Characteristics ± SD		
HbA1c (%)	8.03 ± 0.92	8.37 ± 0.93	8.75 ± 1.00
Fasting glucose (mg/dl)	164.2 ± 48.8	172.7 ± 47.38	185.1 ± 54.58
Weight (kg)	93.3 ± 19.88	93.2 ± 20.38	92.3 ± 21.00
BMI (Kg/m^2)	33.8 ± 6.23	33.6 ± 6.36	33.4 ± 6.65
Waist Circumference (cm)	109.3 ± 13.74	109.5 ± 14.89	109.2 ± 15.80
SBP (mmHg)	131.0 ± 14.46	131.3 ± 14.31	132.3 ± 12.76
DBP (mmHg)	79.7 ± 9.29	78.8 ± 8.87	78.5 ± 8.47
eGFR (mL/min/1.73m^2)	94.4 ± 17.7	90.2 ± 19.7	92.2 ± 20.8
Triglycerides (mg/dL)	190.5 ± 135.91	184.9 ± 126.10	198.8 ± 133.53
HDL-C (mg/dL)	42.8 ± 10.72	44.0 ± 11.34	43.5 ± 11.60
VLDL-C (mg/dL)	36.1 ± 19.84	35.4 ± 19.21	37.7 ± 21.11
LDL-C (mg/dL)	92.8± 34.21	91.7 ± 35.05	93.2 ± 37.07
ALT (IU/L)	30.6 ± 18.3	28.0 ± 16.3	26.8 ± 18.9
AST (IU/L)	23.7 ± 13.9	22.3 ± 11.2	21.5 ± 12.3

Baseline characteristics in efficacy parameters in different HbA1c subsets. Data are Mean ± SD or (%). Abbreviations: ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; DBP=diastolic blood pressure; eGFR=estimated glomerular filtration rate; HbA1c=glycosylated haemoglobin A1c; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; OAM=oral antihyperglycemic medication; SBP=systolic blood pressure; SD=standard deviation; VLDL=very-low density lipoprotein cholesterol.

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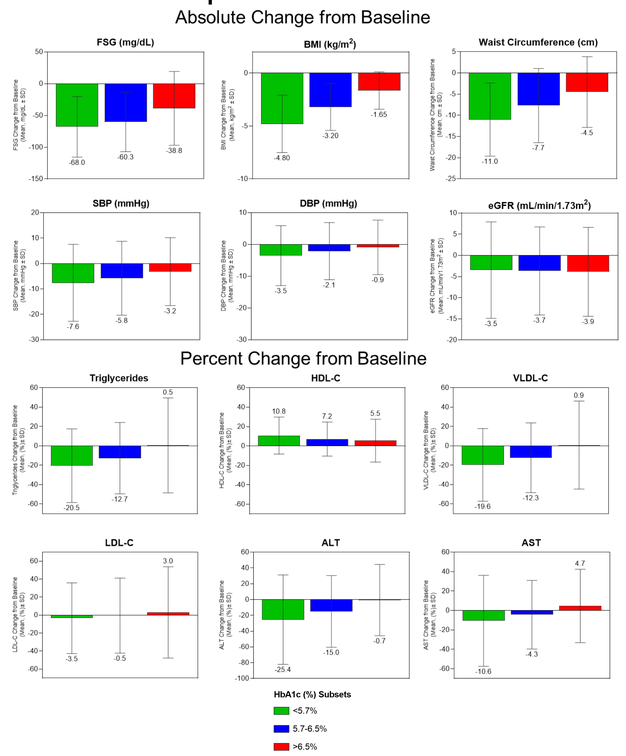
Change from baseline in efficacy parameters by HbA1c subset at week 40

Patients achieving HbA1c <5.7% showed greater reductions in parameters associated with risk of long-term cardiometabolic complications



Absolute and percent change from baseline in efficacy parameters at Week 40 in different HbA1c subsets. Note: change from baseline values represent mean change (SE) at Week 40 (or 42) and not error bar range values. Abbreviations: ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; DBP=diastolic blood pressure; eGFR=estimated glomerular filtration rate; FSG=fasting serum glucose; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; SBP=systolic blood pressure; SD=standard deviation; VLDL=very-low density lipoprotein cholesterol.