Table 2. Baseline Characteristics of Surgery and Non-Surgery Patients After Matching for Age, Sex, BMI, and Blood Pressure

Intervention	Surgery	No Surgery	p Value
Patients (M/W)	385	681	0.689*
Age (years)	40.5	42.4	0.0095
On DM treatment	52	127	0.017*
IFG	16	50	0.033*
HbA1C (%)	6.0	7.8	0.0001
Triglycerides (mg/dL)	131.6	150.9	0.0367
CHD	4	35	0.0001*
Died	12	65	0.0001*
% Died	3.1	9.5	0.0001*
Total Exemptions	83	194	0.013*

BMI = body mass index; CHD = coronary heart disease; DM = diabetes mellitus; IFG = impaired fasting glucose; M = men; W = women.
*Chi-squared test.

achieved significance in matched patients without diabetes (OR, 0.44; 95% CI, 0.19 to 1.00; p = .052). The causes of death were not significantly different between patients who did or did not undergo gastric banding surgery.

The researchers concluded that the prevention of mortality following gastric banding continues for 15 (range, 11–17) years and is associated with the absence of the development of new diseases, in particular DM and CVD, over the same period in patients with and without diabetes. The researchers plan to undertake another round of assessments with the same cohort in 2017.

Characterizing Hypoglycemic Events During Saxagliptin Treatment in Type 2 Diabetes

Written by Emma Hitt Nichols, PhD

Treatment of type 2 diabetes mellitus (T2DM) with saxagliptin increased the risk of major and minor hypoglycemic events, but it enabled more patients to reach an HbA1C target of less than 7% without hypoglycemia. This is according to a subanalysis of the Does Saxagliptin Reduce the Risk of Cardiovascular Events When Used Alone or Added to Other Diabetes Medications? study [SAVOR-TIMI 53; NCT01107886]. Itamar Raz, MD, Hadassah Medical Center, Jerusalem, Israel, presented the results. The main results of this multicenter, randomized, double-blind, placebo-controlled Phase 4 study have been published [Scirica BM et al. *N Engl J Med* 2013].

Hypoglycemia is a serious complication of diabetes treatment, and patients with the greatest risk of hypoglycemia need to be identified. This subanalysis aimed to identify potential predisposing factors for hypoglycemia in patients with T2DM.

The SAVOR-TIMI 53 trial randomly assigned patients with documented T2DM and established cardiovascular disease (CVD) or multiple cardiovascular (CV) risk factors to receive saxagliptin 5 mg/day (dose adjusted for reduced renal function) or placebo. The median duration of follow-up was 2.1 years, with visits every 6 months. The composite primary end points were CV death, myocardial infarction, or ischemic stroke.

Hypoglycemia (any hypoglycemia, minor hypoglycemia, major hypoglycemia, or hypoglycemia requiring hospitalization) occurred more frequently in patients assigned to saxagliptin (Table 1). This excess risk, however, was statistically significant only in the subgroup of patients who were taking sulfonylureas at baseline. Sulfonylurea use without insulin was associated with a significantly higher rate of major hypoglycemia in the saxagliptin group versus the placebo group in patients with a baseline HbA1C level of < 7% (HR, 2.24).

Table 1. Rate of Hypoglycemia by Type With Saxagliptin and Placebo

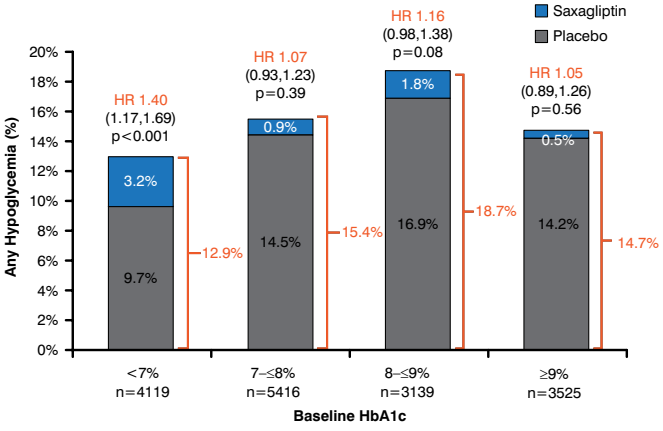
	Saxagliptin	Placebo	p Value
Any hypoglycemia (%)	15.3	13.4	< .001
Minor hypoglycemia (%)	14.2	12.5	0.002
Major hypoglycemia (%)	2.1	1.7	0.047
Hypoglycemia requiring hospitalization (%)	0.6	0.5	0.33

Patients in the saxagliptin arm who were taking at baseline metformin alone, insulin alone, or a sulfonylurea plus insulin or metformin, but not a sulfonylurea alone, were more likely to achieve an HbA1C < 7% without experiencing a hypoglycemic event at 1 and 2 years and at the end of the trial (Figure 1).

In the overall study population, insulin, particularly short-acting insulin, was the strongest predictor for the development of hypoglycemia. In a multivariate analysis, insulin use, decreasing renal function, and increasing disease duration were all independently associated with an increased risk of hypoglycemia.

In conclusion, Prof. Raz stated that the results of this subanalysis of SAVOR-TIMI 53 indicate that insulin therapy is the strongest predictor of hypoglycemia. Treatment with saxagliptin increased the rates of major and minor hypoglycemia in the subgroups noted earlier but not the risk of hospitalization due to hypoglycemia.

Figure 1. Effect of Saxagliptin on Hypoglycemic Events in SAVOR-TIMI 53



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Major episodes of major hypoglycemia were significantly increased in those patients with a baseline HbA1C <7% who were taking a sulfonylurea. Adding saxagliptin to conventional therapy for T2DM increased the proportion of patients whose HbA1C levels were reduced and glycemic targets achieved without hypoglycemic episodes.

Day and Night Closed-Loop Glucose Control Is Feasible in Type 1 Diabetes

Written by Emma Hitt Nichols, PhD

Twenty-four-hour glucose control using a closed-loop system was feasible and resulted in improved glucose control without increasing hypoglycemic events, according to data presented by Lalantha Leelarathna, PhD, University of Cambridge, Cambridge, United Kingdom, from the Closing the Loop in Adults With Sub-optimally Controlled Type 1 Diabetes Under Free Living Conditions study [AP@home02; NCT01666028]. The purpose of the AP@home02 study was to determine the feasibility of using a closed-loop insulin delivery system, combining an insulin pump and continuous glucose monitoring (CGM), for glucose control for 7 days in patients with type 1 diabetes mellitus (T1DM).

In this multinational (3 centers) crossover study, 17 (7 women) adult patients with T1DM were randomly assigned to open-loop or closed-loop glucose control for 7 days and then crossed over to the other modality for another 7 days. Prior to each at-home monitoring period, patients were monitored at the Clinical Research Center (CRC) for 23 hours. All patients received training on CGM and the closed-loop system during the run-in period.

The mean age of the study patients was 34 years, body mass index was 26.2 kg/m^2, and HbA1C was 7.6%. The mean duration of diabetes was 19 years, mean total daily insulin was 40.1 U, and total daily insulin per kilogram per day was 0.53 U.

In the CRC, patients had regular venous sampling, and insulin was given as a bolus 15 minutes before meals using a pump bolus calculator. No bolus was given for snacks during visits for the closed-loop system. At home and work, patients used the closed-loop system without supervision, but 24-hour telephone support was available.

The primary endpoint of glucose within the target range of 3.9 and 10.0 mmol/L during home use was achieved by 75% of patients during the closed-loop phase (95% CI, 62 to 82) compared with 63% during the open-loop phase (95% CI, 55 to 72; p = .006). Mean glucose levels were 8.1 mmol/L in the closed-loop arm compared with 8.8 mmol/L in the open-loop arm (p = .027). When stratified by time of day, the closed-loop system resulted in a greater amount of time in target glucose for both daytime (73%; 95% CI, 63 to 79) and nighttime (48%; 95% CI, 33 to 65) compared with the open-loop system (daytime, 65%; 95% CI, 55 to 71; p = .017; and nighttime, 35%; 95% CI, 28 to 48; p = .013). Insulin infusion with both systems during the home phase is detailed in Table 1.

Table 1. Insulin Infusion With the Closed-Loop and Open-Loop Systems During Home Phase

	Closed-Loop System	Open-Label System	p Value
Total daily insulin (U)	39.1	44.7	0.109
Total daily basal insulin (U)	20.1	18.9	0.017
Total daily bolus insulin (U)	18.9	26.5	0.002
SD of basal insulin (U)	0.7	0.2	< .001

SD = standard deviation.

In the utility analysis, the closed-loop system was operational 83% of the time during the home phase and 98% during the inpatient stay. Undesirable stopping of the closed-loop system occurred due to lack of pump connectivity or CGM availability, the user changing the pump settings, or other unknown reasons.

Adverse events included two severe hypoglycemic episodes; neither was during closed-loop operation, and both patients fully recovered. In one case, the sensor was not working. Four episodes of high glucose occurred because of failure of the insulin infusion system, but there was no ketosis or hospital admission.