trial end, 44.8% of subjects randomized to step-wise required 1 or 2 injections/day.

Step-wise intensification of prandial insulin provides glycemic control comparable to basal-bolus treatment with significantly lower hypoglycemia risk and better patient satisfaction.

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Efficacy and Safety of Dulaglutide Versus Placebo and Exenatide in Type 2 Diabetes (AWARD-1)

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Background and Aims: This phase 3, randomized, parallel-arm study compared the efficacy and safety of 2 doses of dulaglutide (DU) with exenatide (EX) or placebo (PL) in type 2 diabetes patients treated with metformin and pioglitazone.
Materials and Methods: Patients (n=976; mean baseline characteristics: age 55.7 years; HbA1C 8.1%; weight 96.0 kg) were randomized (2:2:2:1) openly to EX 10 mcg BID or, in a double-blind fashion, to once-weekly DU 1.5 mg, DU 0.75 mg or PL. After 26 weeks, the PL group was randomized to DU 1.5 mg or 0.75 mg for 26 additional weeks. All others continued with originally assigned treatments for the study duration (52 weeks). The primary hypothesis was that DU 1.5 mg is superior to PL for change in HbA1C from baseline to 26 weeks.
Results: Both DU (1.5 mg, 0.75 mg) doses were superior to EX and PL, as measured by HbA1C change at 26 weeks (−1.51%, −1.30%, −0.99% and −0.46%, respectively, adjusted $p<0.001$), and to EX at 52 weeks (−1.36%, −1.07% and −0.80%, respectively, adjusted $p<0.001$). The incidence of serious adverse events (AEs) was similar among PL and DU groups. The rank order for incidence of gastrointestinal-related AEs among groups was: EX ∼ DU 1.5 mg > DU 0.75 mg > PL. The incidence of symptomatic hypoglycaemia (≤3.9 mmol/L) was 3.2%, 4.3%, 12.3% and 1.4% for DU 1.5 mg, DU 0.75 mg, EX and PL, respectively.
Conclusions: Both once-weekly DU doses demonstrated superior glycemic control compared with PL or EX, and were well tolerated.

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A Sliding Scale Guideline for Obese, Type 2 Diabetes Patients taking Insulin, While on a Low Carbohydrate Diet

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Eighty-five percent of type 2 diabetes patients are obese. Obesity is a risk factor associated with diabetes development, and insulin use often causes weight gain.

The Dr. Poon Metabolic Diet program involves placing the patient on a low-sugar, low-starch, low-saturated fat and low-sodium diet. Before starting any patient on this diet, we order random glucose and C-peptide tests to assess if the patient still has functioning beta cells. In our past studies, we have found that 85% of our obese type 2 diabetes patients taking insulin actually produced normal amounts of insulin. The causes of their poor glycemic control were their obesity as well as bad food choices.

Since the majority of these patients are producing adequate quantities of insulin, if they lose weight, exercise and follow a diet that is low in sugar and starch, they should not require any extra insulin. The less insulin the patients have to take, the higher the probability of losing weight.

One of the risks associated with placing this type of patient on a low-carbohydrate diet is hypoglycemia. If the patient has to consume sugar to treat hypoglycemic symptoms, it will defeat the purpose of them participating in a low-carbohydrate diet. We therefore developed a guideline to adjust the patient's insulin and sulfonylurea doses in order to prevent hypoglycemia while on this diet. Our results have demonstrated that by following this guideline, our patients are able to achieve both an improved glycemic control and weight reduction without hypoglycemia.

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Efficacy and Safety of Dulaglutide Versus Sitagliptin after 52 Weeks in Type 2 Diabetes (AWARD-5)

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Background and Aims: This phase 3, adaptive, double-blind, parallel-arm trial compared once-weekly dulaglutide (DU) with sitagliptin and placebo in metformin-treated patients with type 2 diabetes. The primary objective was to show non-inferiority of DU 1.5 mg versus sitagliptin on change in HbA1C at 52 weeks.
Materials and Methods: Patients (n=1098, mean baseline characteristics: age 54 years, HbA1C 8.1%, weight 86.4 kg, diabetes duration 7 years) were randomized to DU 1.5 mg, DU 0.75 mg, sitagliptin 100 mg or placebo (replaced with sitagliptin after 26 weeks) in a 2:2:2:1 ratio. The statistical plan allowed for superiority testing once the non-inferiority criterion for each of the doses relative to sitagliptin had been met. The study continued until 104 weeks.
Results: Both DU 1.5 mg and 0.75 mg were superior to sitagliptin in reducing HbA1C after 52 weeks (−1.10%, −0.87%, and −0.39%, respectively, adjusted $p<0.001$). Rates of hypoglycemia (plasma glucose ≤3.9 mmol/L and/or symptoms) were 1.6, 1.7, 1.6 and 1.2 events/patient/year for DU 1.5 mg, DU 0.75 mg, sitagliptin and placebo, respectively. No severe hypoglycemia was reported. The most common treatment-emergent gastrointestinal events for DU 1.5 mg and 0.75 mg, respectively, were nausea (17%, 14%), vomiting (13%, 8%), and diarrhea (15%, 10%). The incidence of discontinuations due to adverse events (most commonly for hyperglycemia) or death was 11.2% (DU 1.5 mg), 7.6% (DU 0.75 mg), 10.2% (sitagliptin) and 16.4% (placebo).
Conclusion: Both once-weekly DU doses demonstrated superior glycemic control to sitagliptin after 52 weeks, with an acceptable tolerability and safety profile.

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Safety and Efficacy of Dulaglutide Versus Sitagliptin after 104 Weeks in Type 2 Diabetes (AWARD-5)

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Background and Aims: This phase 3, adaptive, double-blind, parallel-arm trial compared once-weekly dulaglutide (DU), a long-acting GLP-1 receptor agonist, with sitagliptin and placebo in metformin-treated type 2 diabetes patients.
Methods: The primary time point was 52 weeks; final time point was 104 weeks. Patients (n=1098; mean baseline characteristics: age 54 years; HbA1c 8.1%; weight 86.4 kg; diabetes duration 7 years) were randomized to DU 1.5 mg or 0.75 mg once-weekly, sitagliptin 100 mg daily or placebo (up to 26 weeks).

Results: Similar proportions of DU and sitagliptin patients completed 104 weeks of treatment. Both once-weekly DU (1.5 mg, 0.75 mg) doses were superior to sitagliptin as measured by change in HbA1c at 104 weeks (−0.99%, −0.71% and −0.32%, respectively, adjusted $p<0.001$). Both DU doses were associated with a higher incidence of gastrointestinal (GI) treatment-emergent adverse events (AEs) than sitagliptin. The most common GI AEs for DU 1.5 mg, DU 0.75 mg and sitagliptin, respectively, were nausea (17%, 15%, 7%), vomiting (14%, 8%, 4%) and diarrhea (16%, 12%, 6%). The incidence of GI TEAEs peaked during the first 12 weeks, with no difference between groups after 26 weeks. Weight change was −2.88 kg in the DU 1.5 mg arm, −2.39 kg in the DU 0.75 mg and −1.75 kg for the sitagliptin arm ($p<0.001$ for DU 1.5 mg versus sitagliptin).
Conclusion: Once-weekly DU AEs profile and superior HbA1c control versus sitagliptin after 104 weeks indicate an acceptable benefit/risk profile of DU over a longer time.

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Comparative Safety and Effectiveness of Sitagliptin in Patients with Type 2 Diabetes and Heart Failure

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Background: Sitaglitpin (an oral incretin therapy) is hypothesized to have both cardiovascular and heart failure-specific benefits. The objective of this study was to determine if the use of sitagliptin was associated with any benefit or risk on clinical outcomes in a population-based cohort of patients with type 2 diabetes and incident heart failure.
Methods: Using a large commercially insured US claims database, 11 967 subjects with type 2 diabetes and incident heart failure were identified through physician claims, hospital discharge abstracts and/or ambulatory care visits based on ICD-9 CM codes. Our population-based cohort was followed from January 1, 2004 until death, termination of medical insurance or December 31, 2010. Time-varying multivariable Cox proportional hazards models were used to assess differences in all-cause mortality.
Results: Average age of subjects was 56 years, 39.6% were female and median duration of follow up was 1.94 years. In total, 653 subjects died (5.5%). No association between all-cause death and sitaglitpin use was observed compared to other glucose-lowering agents. After adjustment for demographics, clinical and laboratory data, pharmacy claims, healthcare utilization and time-varying propensity scores, any sitagliptin use was not associated with a statistically significant increase in mortality (adjusted HR 0.64, 95% CI 0.37 to 1.12) compared to no sitagliptin use. Similarly, compared to metformin/sulfonylurea combination therapy, sitagliptin combination therapy was not associated with an increase in mortality (adjusted HR 1.01, 95% CI 0.40 to 2.56).
Conclusion: Sitagliptin therapy was not associated with excess risk of all-cause death among patients with type 2 diabetes and heart failure.

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Pharmacologic Management of Diabetes among Seniors Newly Admitted to Long-term Care Facilities in Saskatchewan

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Objectives: To describe antihyperglycemic medication use within the first 6 months of admission to a long-term care facility (LTCF) in Saskatchewan.
Methods: A retrospective cohort study was performed using health administrative databases in Saskatchewan. Subject inclusion criteria included a first admission to a LTCF between 2003 and 2011 following a 2-year washout period and a diagnosis of diabetes as determined by medication use or physician/hospital claims data. Diabetes medication users were identified by 1 or more dispensations within the first 6 months of LTCF admission.
Results: Of all subjects newly admitted to a LTCF with a diagnosis of diabetes (n=2056), 67.5% (n=1387) used any diabetes medication within 6-month post-admission. Of these, two-thirds (64.0%; n=888) received oral medications only, 20.5% (n=284) received insulin only and 15.5% (n=215) received a combination of insulin and oral medications. Of individuals receiving oral agents, metformin was most commonly dispensed (62.8%; 693/1103) while sulfonylureas were used in 26.3% (290/1103). Use of thiazolidinediones, meglitinides, and acarbose were relatively low and dipeptidyl-peptidase-4 (DPP4) inhibitors were not covered by the provincial drug plan during the observation period. A high rate of glyburide discontinuation (68%; 234/340), defined as $\leq$1 dispensations during the 6-month follow-up period, was observed in those who received this agent within 6 months preceding admission.
Conclusions: Diabetes appears to be frequently managed without pharmacologic therapy in LTCF and medication use appears to generally align with Canadian practice recommendations. However, further studies are needed to confirm these estimates and examine patient and facility-specific characteristics.

Disclaimer: This study is based in part on de-identified data provided by the Saskatchewan Ministry of Health. The interpretation and conclusions contained herein do not necessarily represent those of the government of Saskatchewan or the Saskatchewan Ministry of Health.

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Somatic-Affective Symptoms of Depression Have a Stronger Association with Insulin Resistance than Cognitive Symptoms

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Objective: Somatic-affective depressive symptoms (SA-dep) are more common than cognitive depressive symptoms (C-dep) in cardiovascular disease (CVD), and insulin resistance is critically involved in the development of CVD. We hypothesized that insulin resistance is more strongly associated with SA-dep than with C-dep.
Method: Three hundred twenty-eight cardiac outpatients (mean age = 60) referred for exercise stress testing completed the Beck Depression Inventory II (BDI-II). Blood was drawn to determine homeostatic model assessment (HOMA-IR), a measure of insulin resistance. In principal components analysis (PCA), BDI-II items were forced to load onto 2 components. Adjusting for age, sex, BMI, medication use, smoking, physical activity, diabetes and CVD, GLM analyses were conducted to examine associations between the components and log HOMA-IR.
Results: PCA revealed 9 items loading onto a C-dep component and 10 items loading onto a SA-dep component. When examined separately, both components were significantly associated with log HOMA-IR (ps<.03). However, when including both components simultaneously in the model, only SA-dep remained significantly associated with log HOMA-IR (p=.05). A 1-unit change in C-dep was associated with a .03 change in log HOMA-IR, 95% CI (.005, .06) and a 1-unit change in SA-dep with a .03 change in log HOMA-IR, 95% CI (.01, .06); these values (95% CIs) were .01 (-.02, .05) and .03 (.001, .06), respectively, when both components were in the model.
Conclusion: SA-dep seems more strongly associated with insulin resistance than C-dep. Monitoring SA-dep may be more appropriate than CA-dep among depressed individuals with high insulin resistance.