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Efficacy of Bydureon in Adults with Type 2 Diabetes

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EFFICACY OF BYDUREON IN ADULTS WITH TYPE 2 DIABETES

by

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Abstract

Type 2 diabetes is still rapidly on the rise today, affecting 10.5% of individuals in the United States between the ages 45 to 64 and 18.4% of those between the ages of 65 to 74. In the past two decades, type 2 diabetes has doubled in all age groups. Many adults with type 2 diabetes experience difficulty managing their blood sugars, which can result in a range of further complications. One of the newest treatment options on the market today is a glucagon-like peptide-1 (GLP-1) receptor agonist, Bydureon. Similar to Byetta, Bydureon has a main ingredient of exenatide. It offers once a week dosing as opposed to twice-a-day, which may be more appealing to patients.

The purpose of this study was to examine the efficacy of a newly FDA released medication, Bydureon, once weekly dosage in adults with type 2 diabetes. A descriptive, comparative, retrospective study of 35 patients evaluated efficacy by examining Hgb A1C and body mass index in adults with type 2 diabetes at baseline and 3 months after Bydureon was prescribed. Data were collected by a chart review of records in a primary care practice.

Results demonstrated a statistically significant difference between baseline to 3 month means in both Hgb A1C ($t(34) = -3.05$, $p = .0044$) and BMI ($t(34) = -2.86$, $p = .0072$) for patients using Bydureon.

Health care providers need to individualize the patients' plans of care to address multifactorial areas of their diabetes care and provide them with an opportunity to successfully meet their goals. Practitioners must be knowledgeable about the treatment options available, including the newer GLP-1 receptor agonist, Bydureon and its efficacy for adults with type 2 diabetes.

Chapter One: Introduction

Diabetes mellitus, more commonly referred to as diabetes, is a group of clinically heterogeneous metabolic disorders that are commonly characterized by glucose intolerance resulting from a defect in either the action and/or or secretion of insulin (Jones, Brashers, & Huether, 2010). It is estimated that some 25.8 million people of all ages in the United States (U.S.) have diabetes, approximately 8.3 percent of the total population (National Diabetes Information Clearinghouse [NDIC], 2011). Of these 25.8 million, only 18.8 million people are diagnosed. Diabetes is the seventh leading cause of death in the U.S. and one of the major causes of heart disease, stroke, renal failure, non-traumatic lower-limb amputations, and blindness. It is estimated that by 2030, the estimated worldwide population with diabetes will increase by 60 percent over the 2000 numbers (American Diabetes Association [ADA], 2012). This increase is due to the general population aging, as well as the eating and physical activity habits in the world, with a parallel increase in obesity (Van Dijk, et al., 2011).

Although there is no cure for diabetes, there are a variety of clinical management strategies that can avoid or minimize complications, increase the survival rates, and improve quality of life for the individual with diabetes (American Diabetes Association [ADA], 2012). These strategies include patient education on management and monitoring of blood glucose levels, and maintaining blood glucose within the normal range. A number of antidiabetic medications have been developed to help individuals with type 2 diabetes achieve blood glucose levels. The most recent of these medications are the incretin mimetics including exenatide. Byetta, a twice daily subcutaneous dosage of exenatide was released by the FDA in April of

2005 and its use has been on the rise since then. More recently, in January 2012, Bydureon, an extended release dose of exenatide, was approved by the FDA (Exenatide, 2012).

Purpose

The purpose of this study was to examine the clinical efficacy of Bydureon, once weekly dosage in adults with type 2 diabetes. This descriptive, comparative, retrospective study evaluated medication efficacy by examining Hgb A1C and body mass index in adults with type 2 diabetes at baseline, and then at 3 months after Bydureon was prescribed. The research question was:

Do adult patients with type 2 diabetes who are started on the once weekly dosage of Bydureon have an improved Hgb A1C and BMI over a 3 month period?

Theoretical Framework

The conceptual framework that grounds this study is the health belief model, first developed in 1935 by Kurt Lewin, the Gestalt psychologist (Rosenstock, Strecher, & Becker, 1988). Lewin developed the field theory of decision making and believed that people are viewed as acting in a life space, which is the quantity of all the psychological factors imposing upon a person at any given moment in time. In the 1950s, a group of social psychologists, including Rosenstock, Hochbaum, and Kegels, working for the U.S. Public Health Services, focused on making improvements in preventative health services. They further developed the health belief model while trying to examine why individuals did not participate in prevention and screening programs. In the 1970s and 1980s, this model was expanded by Becker, and the latest changes to the model were done in 1988 (Rosenstock, et al., 1988). The health belief model has been recommended as an applicable and appropriate model for health promotion in individuals with diabetes (Gutierrez & Long, 2011).

The health belief model addresses an individual's perception of the risk of a health problem and the associated assessment of a recommended behavior for managing the problem, which is manifested as a behavior (Rosenstock, et al., 1988). There are three major components of the model: individual perceptions, modifying factors, and likelihood of action (See Figure 1.1). This specific conceptual framework is relevant because medication adherence is frequently assessed and evaluated through the lens of the health belief model. It is apparent that in individuals with diabetes, control is intimately linked to medication adherence, and control of the disease is linked to clinical outcomes, and long-term complications such as renal failure, amputations, diabetic ulcers, and blindness. Improving medication adherence results in tighter glucose control, maximizing the potential for improved outcomes.

Figure 1.1

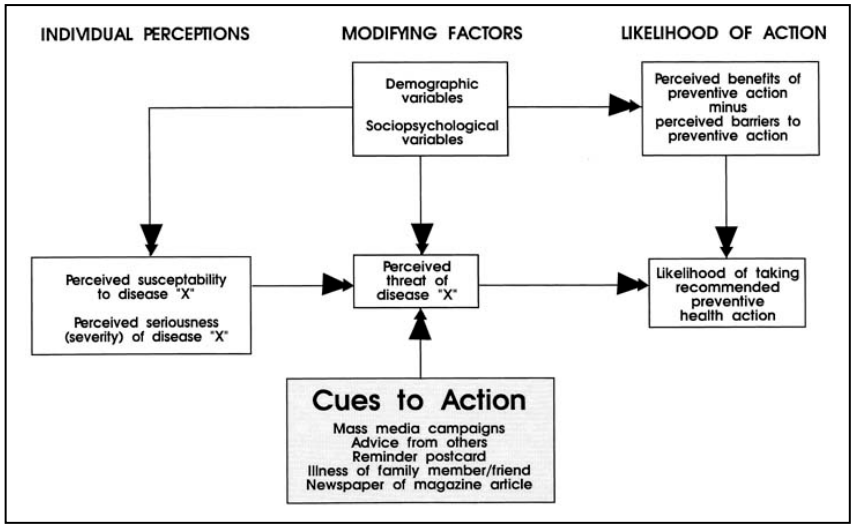

Figure 1.1. From "Basic Elements of the Health Belief Model," by R. Ashford and A.S. Blinkhorn, 1999, *British Dental Journal*, 186, p.436. Copyright 2012. Reprinted with permission.

Individual Perceptions

Individual perceptions are those perceptions of one's susceptibility to the disease or condition and one's perception of the seriousness of the disease or condition if one develops the

condition (Rosenstock, et al., 1988). Perceived susceptibility is one's opinion of the chances or assessment of their risk for developing the condition, in this case, diabetes. In a diabetic individual, perceived susceptibility is determining their beliefs regarding the results of medication non-compliance.

Perceived severity is one's opinion on the severity of a condition and its potential consequences. In a diabetic individual, perceived severity is looking at their beliefs about the severity of their health illness and resulting complications.

Modifying Factors

Modifying factors are demographic and psychosocial variables, perceived threat, and cues to action. Demographics include the individual's age and sex, and psychosocial variables include the individuals personality and social class. Perceived threat is the threat of diabetes itself. Cues to action are factors that may be used to activate the willingness of the person and stimulate the good behaviors. Cues of action stimulates the individuals readiness to act on their given health plan or medication regimen (Kuhns & McEwen, 2011).

Likelihood of Action

Likelihood of action is the likelihood that the individual will take the plan of action and follow through with it. This last component of the health belief model includes an examination of the interplay between perceived benefits of and perceived barriers to the health promoting behavior. Perceived benefits are one's assessment of the positive consequences of adopting the health behavior. In an individual with diabetes, perceived benefits are defined as the individual's overall health and their perception of how the medication regimen will benefit their overall health (Kuhns & McEwen, 2011).

Perceived barriers are one's opinion of the tangible and psychological cost of the advised action (Kuhns & McEwen, 2011). In an individual with diabetes, perceived barriers are the individual's perception of the side effects of the medications, their long term effects, and the difficulty of integrating the medication regimen into their daily life schedule.

Self-efficacy defines the confidence the individual feels in their ability to successfully manage and maintain their health illness. It was introduced to address habitual unhealthy behaviors and the challenges with respect to those behaviors (Kuhns & McEwen, 2011).

Definition of Terms

Diabetes Mellitus

Diabetes mellitus is a condition characterized by hyperglycemia resulting from the body's inability to utilize blood glucose for energy (Jones et al., 2010).

Type 2 diabetes

Type 2 diabetes is a condition characterized by high blood glucose levels or glucose intolerance typically presenting in adulthood and exacerbated by obesity and an inactive lifestyle. This condition results in either a lack of insulin secretion or the inability of the body to use insulin efficiently (ADA, 2012).

Bydureon

Bydureon is a once-a-week dosed incretin mimetic medication used to reduce fasting and postprandial glucose levels (Lippincott, 2012).

Hemoglobin A1C (Hgb A1C)

Hemoglobin A1C is a laboratory measure of an individual's blood glucose level average over a period of two to three months. It is a direct measure of the amount of glucose adhering to

the red blood cell, which is directly proportional to the amount of glucose in the blood (ADA, 2012).

Body mass index (BMI)

Body mass index is a calculated measure used to evaluate body weight relative to a person's height and determines if a person is underweight, normal weight, overweight, or obese. The formula for BMI is: Weight (lb) / (Height (in) x Height (in)) x 703 (ADA, 2012).

Chapter Two: Review of Literature

This chapter begins with a basic overview of diabetes mellitus. Type 1 diabetes mellitus is briefly discussed followed by a thorough discussion on type 2 diabetes mellitus, covering the pathophysiology, prevalence, risk factors, clinical manifestations, evaluation, and treatment including the new incretin mimetic medication, exenatide. Lastly, research on exenatide are examined and summarized.

Diabetes Mellitus

Diabetes mellitus, more commonly referred to as diabetes, is not a single disease but a group of clinically heterogeneous disorders that are classified by glucose intolerance (Jones, et al., 2010). Diabetes consists of several different etiologies of disturbed glucose tolerance and includes many causally unrelated diseases. Disturbance of carbohydrates, fats, and protein metabolism characterizes diabetes as well as chronic hyperglycemia. There are four different categories of diabetes; type 1; type 2; other specific types, generally associated with medications and/or other conditions; and gestational diabetes, which is diabetes diagnosed in and confined to the pregnancy period (ADA, 2012). The most common of the four are type 1 and type 2 diabetes (see Table 2.1 for a general comparison).

Table 2.1

Comparison of Type 1 and Type 2 Diabetes

Feature	Type 1 Diabetes	Type 2 Diabetes
Onset	Sudden	Gradual
Age at Onset	Mostly young	Mostly in adults
Body Habitus	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, decreased or increased
Concordance in identical twins	50%	90%
Prevalence	Less prevalent	90-95% of US diabetics

From Comparison of type 1 and 2 diabetes. Information from http://www.diffen.com/ difference/ Type_1_Diabetes_vs_Type_2_Diabetes

Type 1 Diabetes

Type 1 diabetes, previously known as juvenile diabetes or insulin-dependent diabetes, is the result of the absence of insulin production due to an autoimmune-mediated specific loss of beta cells in the pancreatic islet. A genetic-environmental interaction is thought to be the cause of type 1 diabetes, but it is still unclear. While diagnosed in both children and adults, diagnosis of the disease is most commonly made at the age of 12 years with winter and fall seasonal distribution. Type 1 diabetes mellitus affects 0.17 percent of children in the United States and 10 percent of all the people with diabetes. The staple in the pharmacologic management of type 1 diabetes is the self-administration of insulin (Jones, et al., 2010).

Type 2 Diabetes

The endocrine system is a complex network made up of integrated hormone-producing glands and organs that produce and release various hormones to maintain and control important functions in the body. In the case of diabetes, this network involves insufficient islet B-cell and adipose-tissue responses to chronic fuel surplus, which results in a so-called nutrient spillover,

resistance of insulin, and finally, overall metabolic stress. The final damage includes multiple organs (Nolan, Damm, & Prentki, 2011).

In type 2 diabetes, the body either fails to produce sufficient insulin to meet the body's needs (decreased insulin secretion by beta cells) or insulin target cells ignore the insulin (insulin resistance). In order for the body to utilize glucose for energy, insulin is necessary. When an individual consumes food, the body breaks down all of the sugars and starches into glucose, which is the basic fuel for the cells in the body. Insulin then transports glucose from the bloodstream into the individual cells (Jones, et al, 2010).

Pathophysiology

There have been several different genes identified associated with type 2 diabetes. These include genes that code for beta cell mass, beta cell function, proinsulin and insulin molecular structure, insulin receptors, hepatic synthesis of glucose, glucagon synthesis, and cellular responsiveness to insulin stimulation (Nolan, et al., 2011). In combination with environmental influences, these genetic anomalies result in type 2 diabetes. Although many individuals with risk factors for type 2 diabetes, such as obesity, metabolic syndrome, and hypertension are insulin resistant, only those with a genetic predisposition will develop diabetes mellitus. A suboptimal response of insulin-sensitive tissue to insulin is what defines insulin resistance. Abnormality of the insulin molecule, high amounts of insulin antagonists, down-regulation of the insulin receptor, decreased or abnormal activation of postreceptor kinases, and alteration of glucose transporter proteins all are mechanisms involved in the abnormalities of the insulin signaling pathways and contribute to insulin resistance (Jones, et al., 2010).

Obesity, a major contributor to insulin resistance, is noted in approximately 60 to 80 percent of individuals with type 2 diabetes. Obesity leads to an increased level of adipokines,

hormones produced in adipose tissue, resulting in decreased insulin sensitivity. With a decreased level of insulin sensitivity, there is high risk for developing type 2 diabetes. Also associated with obesity are increased serum free fatty acid and intracellular deposits of triglycerides and cholesterol, usually due to a high caloric and lipid intake. High caloric and lipid intake results in interference with the signaling of intracellular insulin and decreases the responses to insulin in the tissue, causing an alteration in the secretion of insulin within the beta cells, intra-abdominal adipocytes are inflammatory cytokines that further contribute to insulin resistance (Jones, et al., 2010).

An individual may have diabetes for many years with masking of clinical appearance due to compensatory hyperinsulinemia. Compensatory hyperinsulinemia is when the body compensates for a state of elevated insulin in the body. This is required to achieve and maintain a sufficient degree of glycemic control (Edelman & Henry, 2002). Beta cells begin to dysfunction, which then leads to an insulin activity deficiency. Beta cells go through cell exhaustion or undergo cell death. As this process continues, patients then begin to present with some of the clinical manifestations of the disease, and type 2 diabetes is then diagnosed (Jones, et al., 2010). When the disease has gone on unrecognized for many years, complications, such as early stages of microvascular and frank macrovascular disease may be present at the time of diagnosis (Edelman & Henry, 2002).

Glucagon is a very important hormone in the endocrine system that is produced by the alpha cells of the pancreas and acts in the liver to increase blood glucose by acting as an antagonist to insulin. In type 2 diabetes, the pancreatic alpha cells are less responsive to glucose inhibition, resulting in an increased glucagon secretion, resulting in increased hepatic glucose

and subsequent hyperglycemia. Amylin, also released by the beta cells, inhibits functions to inhibit glucagon secretion (Jones, et al., 2010).

Several peptides are involved in the processes of glucose metabolism. Incretins are released from the gastrointestinal tract, in response to food intake, and increases the sensitivity of beta cells to circulating glucose levels, thereby improving insulin responsiveness to meals. GLP-1 is cleaved from proglucagon in the intestinal mucosa, and binds to receptors on beta cells, increasing the synthesis and secretion of insulin in response to glucose levels. Another peptide produced in the gastrointestinal tract and pancreatic islets cells is ghrelin. Ghrelin stimulates growth hormone production; decreased levels of ghrelin have been associated with insulin resistance and increased fasting insulin levels in individuals with type 2 diabetes (Jones, et al., 2010).

Prevalence

Within the United States, type 2 diabetes accounts for approximately 90% of all diabetes cases. Type 2 diabetes is most common among Latinos, Native Americans, Asian Americans, African Americans, Native Hawaiians, other Pacific Islanders, and the aged population (ADA, 2012).

The incidence of type 2 diabetes has doubled in the past two decades. Although the greatest increase has been seen among white men, type 2 diabetes diagnosis remains the most common among black women. There has also been an increase in diagnosis among Native American children aged 15 to 19 and in obese children worldwide (ADA, 2012).

Risk Factors

The most well-recognized risk factors for type 2 diabetes are age, obesity, hypertension, physical inactivity, and family history. Other risk factors still being investigated are elevated C-reactive protein, decreased adiponectin, increased leptin, and increased interleukin 6 (IL-6) (Jones, et al., 2010).

Clinical Manifestations

Type 2 diabetes often has nonspecific clinical manifestations. While this disease may affect individuals younger than age 30 years, it typically afflicts individuals older than 30 years of age. Some of the classic symptoms of type 2 diabetes are polyuria, an increase in urination; polydipsia, an increase in thirst; and polyphagia, an increase in hunger (Edelman & Henry, 2002). Hunger is triggered by the decrease or depletion of insulin resulting in the inability to transport glucose from the intravascular tissue into the cells depleting the muscles and organs of an energy source. Although an individual may experience an increase in appetite in order to satisfy their hunger, weight loss may be noted due to the inability to metabolize glucose affecting utilization of alternative fuels stored in muscle and fat tissue.

Fatigue is also a common feature experienced in type 2 diabetes. Hyperglycemia results in osmotic changes not only in the vasculature but within the ocular tissue as well resulting in visual changes such as diminished visual acuity. Furthermore, type 2 diabetics may result in delayed wound healing and frequent infections such as vaginal and urinary tract infections. Individuals with type 2 diabetes may develop acanthosis nigricans, dark and velvety areas within the folds and creases of the skin, typical of insulin resistance that is caused by changes in keratin in the skin. The presence and severity of symptoms may vary from individual to individual or may be entirely absent (Jones, et al., 2010).

Evaluation

Diabetes should be suspected in the presence of any of the above signs and symptoms. Clinicians should have a high index of suspicion of type 2 diabetes if multiple risk factors are present, even in the absence of signs and symptoms. These individuals should be screened for pre-diabetes, the condition in which an individual has either impaired fasting glucose or impaired glucose tolerance (Edelman & Henry, 2002).

Laboratory evaluation may be a fasting plasma glucose, 2-hour oral glucose tolerance test, and HgbA1c (Jones, et. al., 2010). These tests may be used to diagnose either pre-diabetes or diabetes. Table 2.2 provides the laboratory differentiation between pre-diabetes and diabetes. Pre-diabetes may be manifested as either impaired fasting glucose or impaired glucose intolerance.

Table 2.2

Laboratory Evaluation for Diagnosis of Diabetes

Test	Values for Pre-diabetes	Values for Diagnosis
Random Blood Glucose	Two random test greater or equal to 140mg/dl but less than 200mg/dl	Greater than or equal to 200 mg/dl
Fasting Plasma Glucose	100mg/dl to 125mg/dl	Greater than or equal to 126mg/dl
2-hour post-75Gm Glucose Load	140mg/dl to 199mg/dl	Greater than or equal to 200mg/dl
Hgb A1C	5.7% to 6.4%	Greater than or equal to 6.5%

Information from "Diagnosis and Classification of Diabetes Mellitus," by American Diabetes Association, 2010, *Diabetes Care, 33*, pp.66-67.

Elevated fasting plasma glucose concentration, abnormal oral glucose tolerance test, and symptoms such as polyuria, polydipsia, and polyphagia are included in the criteria for the diagnosis of diabetes. Impaired glucose tolerance resembles diabetes mellitus in that it results

from reduced suppression of hepatic glucose output and a reduction in the function of the pancreatic islet cells. Similar to overt diabetes, individuals with impaired glucose tolerance are at increased risk of cardiovascular disease and premature death (Jones, et al., 2010). These individuals should be informed of their increased risk from their health care provider and should be counseled on effective strategies, such as exercise and dieting, to decrease their risks. These individuals should see their health care provider more frequently to have these tests completed and continue close monitoring of diabetes. Persons, who are diagnosed with type 2 diabetes, should be referred to an endocrinologist for follow up every three to six months for development of a plan of care prescribed by the endocrinologist (ADA, 2010).

Treatment

Treatment of type 2 diabetes is a very important aspect in the overall management of type 2 diabetes. The goal of treatment is to restore near-euglycemia and correct related metabolic disorders. Diet, exercise, and weight loss are an important adjunct to an appropriate medication regimen. While caloric restrictions are the mainstay of an appropriate diet for the type 2 diabetic, minimizing the consumption of refined carbohydrates including processed sugars should also be incorporated as part of the diabetic regimen. A potential benefit of weight loss is a reduction in insulin resistance and increase in insulin sensitivity further improving glucose control. Based on the Medical Nutrition Therapy for Prevention and Treatment of Diabetes, each diet needs to be individualized with a focus on reduction in fats and carbohydrates (Jones, et al., 2010).

Exercise is a very important aspect in individuals with type 2 diabetes. Exercise promotes insulin sensitivity resulting in reductions in glucose levels as well as diminished medication requirements (Nolan, et al., 2011). In addition, exercise reduces serum triglyceride and total

cholesterol levels while increasing high-density lipoprotein levels, enhancing weight loss weight, and an overall feeling of well-being.

When diet and exercise are ineffective in adequately managing diabetes, the use of medications is indicated. Oral medications include sulfonylureas, biguandides, thiazolidinediones, dipeptidyl peptidease-4 inhibitors, and α-glucosidase inhibitors. Sulfonylureas are used to acutely supplement beta cell insulin secretion, whereas biguandides prevent hepatic glucose production and increase the sensitivity of peripheral tissue to insulin. Thiazolidinediones increase insulin sensitivity, especially in adipose tissue. DDP-IV inhibitors increase GLP-1 levels that in turn increase insulin secretion. a-Glycosidase inhibitors delay carbohydrate absorption in the gut and inhibit disaccharides and therefore decrease postprandial hyperglycemia (Nathan, et al., 2009).

While traditionally reserved for use in later stages of type 2 diabetes, the early initiation of exogenous insulin has become more common and suggested (Nathan, et al., 2009). Insulin increases peripheral glucose utilization and therefore decreases hepatic glucose output and lipolysis. Insulin may also be used in conjunction with various combinations of oral medications (Krentz, Patel, & Bailey, 2008). More recently, the discovery of the incretin system has led to the advent of a novel class of anti-diabetic medications known as the GLP-1 receptor agonists, specifically extenatide (Campbell, 2011).

Exenatide

GLP-1 is an amino acid that enhances glucose-dependent insulin secretion as well as other antihyperglycemic functions including suppressing glucagon secretion and delaying gastric emptying thereby slowing carbohydrate absorption into the blood stream (Lippincott, 2012). Exenatide, a GLP-1 receptor agonist, is an injectable synthetic formulation of exendin-4, a

peptide derived from the saliva of the Gila monster. The amino acid sequence of exenatide partially overlaps that of GLP-1 thereby mimicking the effects of GLP-1. GLP-1 activity helps to improve glycemic control whenever blood glucose is elevated and in a fasting state, stimulates glucose-dependent insulin secretion and suppresses inappropriate glucagon secretion, which then decreases hepatic glucose production. In a nourished state, GLP-1 stimulates glucose-dependent insulin secretion, suppresses postprandial glucagon secretion, which decreases hepatic glucose production, improves first-phase insulin response, slows gastric emptying, and reduces food intake (Bydureon, 2012).

Exenatide is contraindicated in patients with hypersensitivity to exenatide or its components, type 1 diabetes or diabetic ketoacidosis, and individuals with end-stage renal disease or severe gastrointestinal disease. While adequate studies of exenatide use during pregnancy are limited, rat studies did result in fetal abnormalities. Thus, exenatide is a pregnancy category C drug that should only be used during pregnancy if the potential benefit outweighs the potential fetal risk. Furthermore, exenatide should be used cautiously during breastfeeding (Lippincott, 2012).

Adverse reactions to exenatide include dizziness, headaches, weakness, anorexia, diarrhea, dyspepsia, nausea, pancreatitis, vomiting, reflux, hypoglycemia, excessive sweating, prutitis, urticaria, rash, injection site reaction, angioedema, and anaphylaxis. Common drug interactions may include acetaminophen, digoxin, lisinopril, lovastatin, and sulfonylureas (Lippincott, 2012).

Important considerations for exenatide involve assessing renal and gastrointestinal function before and frequently during treatment (Exenatide, 2012). Glucose levels should be monitored regularly and glycosylated hemoglobin levels obtained periodically. Exenatide should

be discontinued if pancreatitis is suspected. When prescribing exenatide, the patient should be informed of the risks of use as well as a review of the proper use and storage of dosage pen and pen needles. The patient should be informed as to the timing of administration of exenatide with respect to the morning and evening meal.

Patients should be made aware that exenatide may decrease appetite, food intake and body weight and does not warrant a change in dosage. Individuals on exenatide need to be educated that severe, persistent, unexplained abdominal pain or vomiting needs to be reported to health care provider immediately. Steps for managing hypoglycemia need to be reviewed with individuals taking exenatide. The storage of exenatide is very important and needs to be reviewed with the individual. Patients should be educated on infection prevention of local site injections (Exenatide, 2012).

Preparations

Exenatide is available in two preparations, Byetta and Bydureon. Byetta is prepared as 5 mcg/dose and 10 mcg/dose in 1.2 ml and 2.4 ml prefilled pens respectively. Byetta is administered subcutaneously within 60 minutes before the morning and evening meals. The individual is usually initiated on a 5 mcg subcutaneous dose twice daily and then escalated to a 10 mcg subcutaneous dose twice daily after one month. Byetta may be administered in the traditional subcutaneous sites such as the thigh, abdomen, or upper arm. Furthermore, Byetta should be stored in the refrigerator at 36 to 46 degrees Fahrenheit and should be discarded after 30 days, even if it is not completely empty (Exenatide, 2012).

Bydureon is the newly approved extended-release formulation of exenatide. Bydureon is available as a single dose weekly injection of 2 mg. Bydureon is supplied as a self-contained kit which includes a 2 mg dose of powdered Bydureon that is then suspended in an accompanying

prefilled syringe of diluent before injection. This medication is administered once weekly and can be administered at any time during the day, with or without meals, provided it is administered the same day every week. Once again, this subcutaneous injection can be given in the thigh, abdomen, or upper arm and should be stored in the refrigerator at 36 to 46 degrees Fahrenheit and discarded after 30 days, even if it is not completely empty (Bydureon, 2012).

Research on Exenatide

A series of studies, called DURATION, have been completed. These studies-examine the efficacy of Byetta and/or Bydureon and/or other hypoglycemic agents.

DURATION-1 was a randomized, multicenter, comparator-controlled, open-label trial that compared Byetta versus Bydureon in 295 patients with type 2 diabetes. This study focused on Hgb A1C, fasting plasma glucose, and body weight. Bydureon elicited sustained improvements in glycemic control and body weight throughout the 52-week study, and patients who switched from Byetta to Bydureon experienced further improvements in Hgb A1C and fasting plasma glucose (Buse, et al., 2010).

DURATION-2 compared the efficacy and safety of Bydureon versus Sitagliptin or Pioglitazone as an adjunct to metformin for type 2 diabetics. This was a 26-week randomized, double-blinded, double-dummy, superiority trial that included 514 participants. Addition of Bydureon to metformin achieved the goal of optimal glucose control more than an addition of maximum daily doses of either Sitagliptin or Pioglitazone (Bergenstal, et al., 2010).

DURATION-3 compared exenatide once weekly with insulin glargine in patients with type 2 diabetes. This study was an open-label randomized trial that included 456 patients, 233 on Exenatide and 223 on insulin glargine. Hgb A1C was monitored throughout this 26 week study and the interpretation from this study was that Bydureon is an important therapeutic option for

type 2 diabetics for whom risk of hypoglycemia, weight loss, and convenience are particular concerns (Diamant, et al., 2010).

DURATION-4 compared the efficacy and safety of Bydureon versus metformin, Pioglitazone, and Sitagliptin used as monotherapy in drug-naïve type 2 diabetic patients. There were a total of 820 participants in this study that were monitored over 26 weeks in this double-blind study. The results showed that Bydureon was non-inferior to metformin, but not Pioglitazone and was superior to Sitagliptin with regards to reduction of Hgb A1C. Bydureon and Metformin showed similar improvements in blood sugar control along with weight reduction benefit and no increased risk of hypoglycemia (Russell-Jones, et al., 2011).

DURATION-5 compared the effects of once-weekly Bydureon versus twice daily, Byetta for treatment of patients with type 2 diabetes. This study was conducted in 43 sites throughout the United States, with 252 type 2 diabetic participants, and it was a 24 week, randomized, open-label, comparator-controlled study that focused on glycemic control, body weight, and safety with exenatide. Hgb A1C was measured from baseline to week 24 and in conclusion, Bydureon resulted in superior glycemic control, with fewer side effects than Byetta did in patients with type 2 diabetes (Blevins, et al., 2011).

Lastly, DURATION-6 study was the most recent study that was completed on exenatide. This was a 26 week open-label, multicenter clinical study that compared Bydureon to Victoza when administered at the maximum dosage. This study looked at Hgb A1C and results showed that both treatment groups demonstrated a reduction in glucose and weight loss, but this trial did not meet the prespecified primary endpoint that once-weekly injections of Exenatide were noninferior to daily injections of Victoza (Buckley, 2011).

Since Bydureon trials in DURATION studies have reported positive clinical outcomes, Bydureon dosed once a week may be more convenient and as effective as other GLP-1 receptor agonists. This research will provide information for the advanced practice nurse in a family care setting to educate patients on making decisions as to the medication regimen for managing their type 2 diabetes. This study determined the effectiveness of Bydureon as related to Hgb A1C and BMI results over a 3 months period, from a small sample in a primary care setting. This aids the advanced practice nurse in developing a successful treatment plan and provided knowledge on Bydureon effectiveness.

Chapter Three: Methodology

This chapter includes a description of the research design, the sample, and setting for the study. Following is a discussion of the methods for data collection, tools for measurement, statistical analysis and the protection of human subjects.

The purpose of this study was to examine the efficacy of Bydureon, once weekly dosage in adults with type 2 diabetes. This descriptive, comparative, retrospective study evaluated the medication efficacy by examining Hgb A1C and body mass index in adults with type 2 diabetes at baseline, and then 3 months after Bydureon was prescribed. The research question was: Do adult patients with type 2 diabetes who are started on the once weekly dosage of Bydureon have an improved HGB A1C and BMI after a 3 month period?

Study Design

A descriptive, comparative, retrospective design comparing baseline to 3 month of Hgb AIC and BMI was used to examine once weekly dosing of Bydureon in adults with type 2 diabetes. Outcomes measured were Hgb A1C and BMI.

Sample and Setting

Based on a power analysis, a convenience sample size of 35 patients over the age of 18 with type 2 diabetes who were started on the newly released GLP-1 were selected for this study. This provided sufficient statistical power to determine large effect sizes in the two variables, Hgb A1C and BMI by using a paired t-test (alpha=0.05; beta=0.2). Participants were recruited from a local endocrinology clinic in northeast Florida.

Inclusion criteria were males and females with type 2 diabetes who are 18 years-of-age or older, who have been on Bydureon for at least 90 days, with a Hgb A1C and BMI that were recorded in their chart before they started on Bydureon and then 3 months after treatment was

started. Exclusion criteria were any male or female with type 1 diabetes, any individual being treated with insulin other than basal and brief course of short-acting insulin.

It was unknown in this study if these patients were newly diagnosed with type 2 diabetes, the type 2 diabetes diagnosis date, and the exact reason why Bydureon was the medication of choice for the particular participant.

Recruitment

Every clinical medical record where Bydureon was prescribed was reviewed for inclusion and exclusion criteria. The physician and/or nurse practitioner at this individual clinic advised the primary investigator when they ordered Bydureon for a patient and data collection began with chart review to determine if they met both inclusion and exclusion criteria. If they met both inclusion and exclusion criteria, then data collection began with a chart review. IRB reviewed the study, it was deemed exempt. As this was a retrospective chart review, individual consent was not necessary.

Procedures

Demographic data, information about use of Bydureon, and laboratory and anthropological measurements were gathered. Demographic data included date of birth, gender, and date Bydureon was started. All data was gathered and placed into a flow chart. Retrospective chart review provided the laboratory data (Hgb A1C) and anthropological measurements (height and weight). BMI was calculated based on the patient's height and weight. The location where the patient had their labs drawn for their Hgb A1C varied depending on their insurance. The clinic has a contract with some insurance companies to draw labs in the office and others were sent out to have their labs drawn, however, these details were not obtained on

the individual participants. If labs were drawn outside of the clinic, the results were sent to the clinic and then inserted into their computerized chart.

Data Collection

Data collection for this study was a retrospective medical chart review for the clinical quantitative outcomes. When starting the initial data collection, the patient's medical records were reviewed by the investigator, retrospectively. Data were collected on a flow chart and kept in a secure location without patient identifiers. A baseline Hgb A1C and BMI, as defined above was calculated from weight and height measurements from the initial visit when the medication was prescribed by the health care provider. Serial data was further obtained from records of the patient's at 3 month follow up visits after being started on Bydureon. These clinical outcomes were also documented in a computerized spreadsheet by the investigator. Patients were numbered one through thirty five.

Statistical Analysis Plan

Descriptive statistics were used to characterize the sample with respect to the lab and demographic variables related to Bydureon use. A distribution analysis and change analysis were performed and looked at age, baseline BMI, 3 month BMI, baseline Hgb A1C, and 3 month Hgb A1C. A paired t-test was used to determine if there was a difference in before starting on Bydureon and after 3 months of being on Bydureon, for both Hgb A1C and BMI.

Protection of Human Subjects

Data collected were held confidential and no names or personal information were disclosed. Approval from the University of North Florida Institutional Review Board was obtained prior to undertaking the study (see Appendix A). The study was deemed exempt by the UNF IRB. When collecting Hgb A1C and BMI data, the medical record was identified by only a

number and initials on a spreadsheet. Data were kept in a spreadsheet on a password coded computer accessible only to the investigator.

Chapter Four: Results

This chapter includes the statistical findings of this study. Demographic information is first summarized. Following the demographic information, inferential statistics of the study are presented.

As mentioned in chapter three, the purpose of this study was to examine the efficacy of Bydureon, once weekly dosage in adults with type 2 diabetes. This descriptive, comparative, retrospective study evaluated the effects of Bydureon by examining Hgb A1C and BMI in adults with type 2 diabetes at baseline and then again 3 months after Bydureon is started. Participants were from a local endocrinology clinic in northeast Florida. The retrospective chart reviews were completed in 2013 at Northeast Florida Endocrine and Diabetes clinic in Jacksonville, Florida.

Characteristics of the Sample

Participants were 33 to 84 years old. All participants had been diagnosed with type 2 diabetes for at least 90 days but the exact duration of diabetes was not obtained. There were 17 males and 18 females that participated in this study, for a total of 35 participants. Demographic data that was obtained was gender and age and is summarized in Table 4.1.

Descriptive Data Analysis

Lab data collected was BMI, baseline and at 3 months, and Hgb A1C, baseline and at 3 months. The BMI ranged from 21.58kg to 60.82kg at baseline and 21.48kg to 60.80kg at 3 months. The Hgb A1C ranged from 5.7 to 14.0 at baseline and 5.5 to 12.2 at 3 months (see Appendix B). All but 7 subjects had a decrease in BMI. All but 7 subjects had a decrease in Hgb A1C (see Table 4.3). Only one subject had an increase in both BMI and Hgb A1C at 3 months after starting Bydureon. Only one subject dropped a whole category, from obese class I to overweight. One patient was an outlier, and was classified as not overweight and had a normal

BMI at baseline and 3 months. Three subjects Hgb A1C changed from high (>6.5%) to normal (<6.5%) (see Table 4.2).

Table 4.1

Description of the Sample (n=35)

Characteristics	N	%
Gender		
Female	18	51.4
Male	17	48.6
Age		
30-39	2	5.71
40-49	7	20
50-59	12	34.28
60-69	10	28.57
70-79	3	8.57
80-89	1	2.85

Table 4.2

Description of Baseline Variables (n=35)

Baseline Variables	N	%
Hgb A1C		
< 6.5%	8	23
> or = 6.5%	27	77
BMI		
Not overweight	1	3
Overweight	8	23
Obese Class I	12	34
Obese Class II	10	29
Obese Class III	4	11

Table 4.3

Hgb A1C Change (baseline to 3 months) (n=35)

Hgb A1C Change (baseline to 3 months)	N	%
Hgb A1C		
High to normal	3	9
Same (high or normal, without worsen)	25	71
Normal to High	0	0
Worsened	7	20

A distribution analysis was completed to determine the distributions of age, baseline BMI, 3 month BMI, baseline Hgb A1C, and 3 month Hgb A1C. A change analysis was performed to determine the change from baseline to 3 months in both the BMI and Hgb A1C.

Figure 4.1

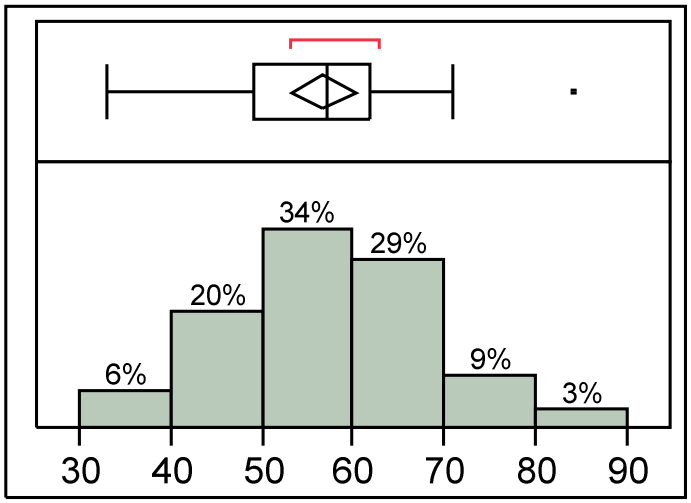

*Figure 4.1.*Age distribution of the participants from the study. Total of 35 participants. The Average age was 56.6. Standard deviation was 10.07. Developed by Dr. Peter Wludyka, Statistician.

Table 4.4

Descriptive Statistics BMI and Hgb A1C(n=35)

	M(SD)		M(SD)
BMI		Hgb A1C	
Baseline	34.89(8.16)	Baseline	7.65 (1.61)
3 Months	34.52 (8.01)	3 Months	7.27(1.42)
Change	-0.37(0.77)	Change	-0.37(0.72)

Based on the distribution analysis and the analysis of change, the mean baseline BMI was 34.89. The mean 3 month BMI was 34.52. The change was a decrease of 0.37 in BMI from baseline to 3 months after being on Bydureon. Anyone with a BMI greater than 30 is considered obese. Both mean baseline and 3 month BMI are categorized as obesity class I according to the Center for Disease Control and Prevention. Class I obesity is BMI 30 to 34.9. (CDC, 2014). The mean baseline Hgb A1C was 7.65. The mean 3 month Hgb A1C was 7.27. The change was a decrease of 0.37 in Hgb A1C from baseline to 3 months after being on Bydureon. (See Table 4.4). Both mean baseline and 3 months Hgb A1C are classified as high. The goal for a patient with type 2 diabetes is a Hgb A1C less than 6.5%, according the American Association of Clinical Endocrinologists and American College of Endocrinology (Handelsman et al., 2011).

Inferential Data Analysis

Paired t-tests

A paired t-test determines whether a sample of matched pairs of similar units differ from each other in a significant way under the assumption that the paired differences are independent and identically normally distributed. In this study, by comparing the same patients BMI and Hgb A1C at baseline and 3 months into their Bydureon treatment, each patient was used as their own control. There was no other control group used for this study. With a paired t-test, the statistical power increases just because the random between-patient variation has been eliminated. The

paired t-test shows statistical significance between baseline to 3 months in both BMI and Hgb A1C on patients that are taking Bydureon. See Table 4.5 for paired t-test results for both BMI and Hgb A1C.

Table 4.5

Paired T-test results: Difference baseline to 3 months (BMI and Hgb A1C)

	Baseline M(SD)	3 month M(SD)	t(DF)	p
BMI	34.89(8.16)	34.52(8.01)	-2.86(34)	0.0072
Hgb A1C	7.64(1.61)	7.27(1.42)	-3.05(34)	0.0044

Note. t=paired t test.

Research Question

The research question was:

Do patients who are started on the once weekly dosage of Bydureon have an improved Hgb A1C and BMI over a 3 month period?

Summary

After reviewing all of the descriptive and inferential statistical analysis it can be concluded that there is a difference in the means of BMI and Hgb A1C over a 3 months period for those on Bydureon. The results were statistically significant and this study showed that the participants had a decrease in both BMI and Hgb A1C over a 3 months period while taking Bydureon.

Chapter Five: Discussion

This chapter provides a discussion of the results regarding BMI and Hgb A1C at baseline and at 3 months in adults with type 2 diabetes after starting on the newer GLP-1 receptor agonist, Bydureon. Following this discussion, the limitations of the study will be examined. After the limitations of the study, the implications for practice and recommendations for future research will be provided.

Discussion

Results from this study do show a reduction in Hgb A1C and BMI in the majority of patients that were taking Bydureon, after only three months of weekly doses. This indicates that the medication has a positive effect on adult patients with type 2 diabetes. When compared to other studies that have been done on Bydureon, the results to this study are very similar. The DURATION-1 study was a three year study that showed patients receiving Bydureon experienced a significant reduction in Hgb A1C (1.6 percentage points) and weight (5.1 pounds) when compared to baseline (Buse, et al., 2010). With a longer duration to follow the participants in this research study on the efficacy of Bydureon, it would be expected to have greater outcomes like the DURATION-1 study. Compared to Lantus, the DURATION-3 study showed that at 84 weeks, patients treated with Bydureon experience a significantly greater Hgb A1C reduction from baseline as well as a weight loss while taking the medication versus the patients that were on Lantus experienced a weight gain (Diamant, et al, 2010). This again is similar to the results that were found in this study, when looking at Bydureon independently.

This study is clinically significant because there are a large number of individuals today with type 2 diabetes. With the number of patients with type 2 diabetes on the rise, health care

providers can use this information, knowing that this medication decreases Hgb A1C and BMI, and use it when trying to find the appropriate diabetes treatment regimen for their patients.

Limitations

Although the study showed significant differences between HgbA1C and BMI when taking Bydureon, several potential limitations warrant mention. Some of the limitations in this study were medications, lifestyle, medical history and number of participants.

Medications

This study could have been improved if the patient's complete medication list was reviewed prior to accepting them to participate in the study. Certain medications that could have had an impact on the participant's results were medications such as weight loss medications, steroids, and other diabetic medications. If a participant was taking a weight loss medication, the results of the BMI would be not a good reflection as to the improvements of weight loss from Bydureon alone. Another thing that could have been taken into consideration in this study was compliance and adherence to therapy and/or proper use of medication, as this was not studied.

Lifestyle

This study could have been improved if patients' lifestyles were taken into consideration. Patients' BMI and HgbA1C are both impacted greatly in their day to day living and habits. Healthy eating habits and daily exercise may help to decrease or control patient's BMI and HgbA1C, as well many of the complications that are associated with type 2 diabetes. Also, an individual's level of stress could impact their BMI. Had all of these components been assessed during this study, more accurate results could have been produced.

Medical history

The only thing reviewed in the participants medical history was their diagnosis of type 2 diabetes. The date of type 2 diabetes diagnosis would have been beneficial to document on each participants. A thorough medical history review to improve this study would have been beneficial. Medical conditions that may have affected the results are history of bariatric surgery, certain cancers, particularly pancreatic cancer and chronic GI complications.

Participant Number

Based on a power analysis, the minimum number of subjects I needed for this particular study was 35 and the number of subjects was 35. With a larger sample size, there would have been a stronger power, and therefore, more conclusive results with this study on the efficacy of Bydureon.

Implications for Practice

It appears that Bydureon does have a positive effect on both Hgb A1C and BMI after only three months. This is consistent with the research that compares this medication to other medications on the market today. As practitioners, it is imperative that treatment of type 2 diabetes is not pharmaceuticals alone. Patients should be educated on healthy eating habits and healthy doses of exercise because from the research that was done as well as other research on type 2 diabetes, it is apparent that patients with type 2 diabetes are typically overweight or obese. During dietary counseling, encouraging the patient to minimize carbohydrates would be a helpful step in managing their type 2 diabetes. Patients need to be educated that their diabetes medication is based on the amount of carbohydrates at each meal, therefore if the individual eats more carbohydrates than they should, the diabetes medication will not be as effective and therefore blood sugars may be uncontrolled. Creating your plate and being mindful of what you

eat is a good step forward when trying to manage your blood sugars. Encouraging these patients to keep a dietary log and record their meals would be a good way for patients to be more mindful of what they are consuming as well as be able to share with their practitioners during their visit in the clinic. Portion control would be vital to discuss with patients that have type 2 diabetes and are overweight or obese as well. The amount of food one eats is closely related to their blood sugar control. Measuring foods would be important to review with patients with type 2 diabetes in order to manage portion control. If the patient is trying to lose weight and manage their diabetes, as a practitioner, Bydureon may be a good selection for their diabetes management. Twenty eight out of the thirty five participants in this study had a decrease in BMI during a three month period after starting on Bydureon. The study does not reveal why the other seven participants did not have a decrease in BMI. Twenty eight out of thirty five participants also had a decrease in Hgb A1C in three months on Bydureon. The study does not reveal why the other seven participants did not have a decrease in Hgb A1C. Compliance and medical conditions would be worth looking into with these select participants that did not successfully progress in their treatment as research has demonstrated in the past.

Bydureon is administered as a subcutaneous injection. With this being known, ease of use is very important for practitioners to be aware of. Like similar medications for diabetes, for example DPP-4 inhibitors, that are administered orally, the only route for Bydureon is via subcutaneous injection. It is the practitioners' responsibility to make sure the patient is comfortable with administration of the medication. Bydureon is only administered once weekly, unlike a patient taking oral form of medication for diabetes is responsible for taking it daily and sometimes twice daily. Compared to the twice daily Byetta, Bydureon can be administered at any time of the day and does not need to be administered with meals. Byetta is a pre-filled pen

device and Bydureon is more complicated with a system that requires assembly. Practitioners prescribing Bydureon must take this into consideration because people with vision problems or limited manual dexterity may find Bydureon system difficult to assemble.

Future Research

In view of the complexity of type 2 diabetes and the current treatment regimens available, more research needs to be done regarding appropriate treatment for individual patients. This study can benefit patients with type 2 diabetes, as Bydureon is another treatment option for available and this study provides some basic knowledge on the short-term effectiveness of this medication. Future research that would be beneficial would be a study on the ease of use of Bydureon to determine if patients are able to properly use the medication and their comfort levels with the once weekly injection. This could be concluded by return demonstration and personal surveys. Some information that would be beneficial to know regarding ease of use would be if the patient had ever administered a subcutaneous injection before, the patients feelings regarding preparation of Bydureon vial and syringe, do they administer injection themselves and if so, ease of administering injection to self, how compliant they are with administering their once weekly injection, have they ever missed doses, how they learned how to administer their first Bydureon injection and any concerns or suggestions they have regarding Bydureon injections. Incorporating patient's lifestyle would be beneficial in future Bydureon research since eating habits and exercise are a huge part of diabetes management. Patients could be educated on health eating habits and exercise by their provider and then be required to log their daily eating habits and exercise for the duration of the study while they are taking Bydureon. Further research that would be beneficial in health care today would be looking at patients on Bydureon with different medical conditions; such as HTN or

hyperlipidemia and determine if the effectiveness of the medication with individuals with these commonly diagnosed medical conditions. A multivariate study would be imperative to future research by looking at more than one outcome, such as incorporating age, gender, and even ethnicity to determine if they are statistically significantly in the outcome of patients taking Bydureon.

Conclusion

Today, approximately 8.3% of the population in the United States have been diagnosed with diabetes and that number is on the rise. The International Diabetes Federation Diabetes Atlas is expecting the total number of individuals with type 2 diabetes to rise to 552 million by 2030 (Hilaire & Woods, 2013). Health care providers need to individualize the patients' plans of care to address multifactorials areas of their diabetes care and provide them with an opportunity to successfully meet their goals. Practitioners must be knowledgeable about the treatment options available, including the newer GLP-1 receptor agonist, Bydureon and its efficacy for adults with type 2 diabetes. Based on the research question, patients started on weekly dosage of Bydureon do have a statistically significant improvement in Hgb A1C and BMI over a 3 month period.

Appendix A

IRB Approval Letter

UNF
UNIVERSITY of NORTH FLORIDA
Office of Research and Sponsored Programs
1 UNF Drive
Jacksonville, FL 32224-2665
904-620-2455 FAX 904-620-2457
Equal Opportunity/Equal Access/Affirmative Action Institution

MEMORANDUM

DATE: September 18, 2013

TO: Ms. Katie Fetter

UNF IRB Number: 344783-5
Amendment Approval: 09-18-2013
Expiration Date: 02-18-2014
Processed on behalf of UNF's IRB KLC

VIA: Dr. Cynthia Cummings
Nursing

FROM: Dr. Krista Paulsen, Chairperson
On behalf of the UNF Institutional Review Board

RE: Amendment review by the UNF Institutional Review Board IRB#344783-5:
"Efficacy of Bydureon in Adults with Type 2 Diabetes"
Original approval: 2/18/2013

This is to advise you that the proposed modifications to your project, "Efficacy of Bydureon in Adults with Type 2 Diabetes" were reviewed and approved on behalf of the UNF Institutional Review Board. Because of the changes, the review type for your project was changed to Expedited category 5. The approved amendments include the following:

1. Removal of all interaction or intervention with participants (surveys will no longer be conducted and research activities include a retrospective chart review of individually identifiable patient medical records which are considered private).
2. Waiver of consent approved for study
3. Title changed to "Efficacy of Bydureon in Adults with Type 2 Diabetes"
4. Updated protocol documents to reflect amended procedures

This study was originally approved by the IRB on 2/18/2013 for a period of one year. Please submit a Status Report for continuing review to the UNF IRB prior to 1/18/2014 if your study will be continuing past the 1-year anniversary of the approval date. *We suggest you submit your status report 11 months from the date of your approval date as noted above to allow time for review and processing.* When you are ready to close your project, please complete a Closing Report Form which can also be found in the documents library called "Forms and Templates" in IRBNet. The status report and updated documents or closing report will need to be added via a new package in IRBNet. All records relating to this research shall be retained for at least 3 years after completion of the research. Data containing protected health information are to be retained for 6 years.

This approval applies to your project in the form and content as submitted to the IRB for review. Any variations or modifications to the approved protocol and/or informed consent forms as they relate to dealing with human subjects must be cleared with the IRB prior to implementing such changes. Any unanticipated problems involving risk and any occurrence of serious harm to subjects and others shall be reported by completing this form and sending it promptly to the IRB within 3 business days. When you are ready to close your project, please complete a Closing Report Form.

CITI Course Completion Reports are valid for 3 years. Katie's completion report is valid through 1/21/2015 and Dr. Cummings' completion report is valid through 4/19/2014. The CITI training for renewal will become available 90 days before your CITI training expires. Please renew your CITI training within that time period by following this link: http://www.citiprogram.org/. Should you have questions regarding your project or any other IRB issues, please contact the research integrity unit of the Office of Research and Sponsored Programs by emailing IRB@unf.edu or calling . This letter will be retained within UNF's records. All records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner.

UNF IRB Number: 944793-5
Amendment Approval: 02-18-2013
Expiration Date: 02-18-2014
Processed on behalf of UNF's IRB KLC

Appendix B

Data collection table:

#/ Initals	Type 2 Diabetic	Age/Gender	Bydureon Start Date	Baseline BMI	3 month BMI	Baseline Hgb A1C	3 month Hgb A1C
1-S.L.	Yes	50/Male	5/20/2013	27.38kg/m2	27.47kg/m2	9.1	8.8
2-A.R.	Yes	36/Female	7/17/2012	28.9kg/m2	28.9kg/m2	5.9	5.8
3-D.M.	Yes	48/female	10/29/2012	43.26kg/m2	42.47kg/m2	8.3	7.7
4-C.W.	Yes	48/Male	2/4/2013	46.51kg/m2	43.11kg/m2	8.3	8.5
5-K.Q.	Yes	47/Female	11/2/2012	36.56kg/m2	36.43kg/m2	5.8	5.7
6-D.W.	Yes	51/Male	4/3/2013	33.41kg/m2	32.9kg/m2	6	6.1
7-J.R.	Yes	59/Female	10/16/2012	36.21kg/m2	35.08kg/m2	8	8.2
8-R.G.	Yes	61/Female	6/19/2012	28.87kg/m2	27.7kg/m2	6.7	6.2
9-G.A.	Yes	57/Male	3/21/2013	60.14kg/m2	59.95kg/m2	7.3	6.2
10-L.B.	Yes	46/Female	11/26/2012	34.51kg/m2	33.83kg/m2	7.5	7.2
11-T.C.	Yes	63/Male	4/11/2013	28.5kg/m2	28.28kg/m2	11.1	9.5
12-D.G.	Yes	48/Male	4/1/2013	28.35kg/m2	28.2kg/m2	8.4	6.9
13-V.M.	Yes	55/Female	2/1/2013	30.79kg/m2	29.96kg/m2	6.3	5.9
14-R.M.	Yes	65/Male	1/17/2013	32.69kg/m2	33.38kg/m2	6	6.3
15-S.R.	Yes	57/Female	9/7/2012	25.45kg/m2	24.84kg/m2	6	5.8
16-V.S.	Yes	66/Female	11/19/2012	31.46kg/m2	32.3kg/m2	5.7	5.5
17-H.S.	Yes	84/Female	1/4/2013	30.71kg/m2	30.31kg/m2	6.7	6.5
18-K.K.	Yes	63/Female	4/5/2012	36.48kg/m2	36.8kg/m2	7.2	6.5
19-E.B.	Yes	61/Male	3/12/2013	21.58kg/m2	21.48kg/m2	14	12.2
20-	Yes	55/Male	3/4/2013	29.41kg	29.41kg	7.9	8

S.P.				/m2	/m2		
21-C.B.	Yes	49/Female	2/26/2013	38.77kg/m2	38.49kg/m2	7.2	7
22-M.C.	Yes	71/Male	3/7/2013	60.82kg/m2	60.80kg/m2	6.7	6.5
23-B.W.	Yes	59/Male	2/26/2013	33.51kg/m2	33.25kg/m2	7.2	6.9
24-J.W.	Yes	60/Female	3/7/2012	35.61kg/m2	34.19kg/m2	7.6	6.4
25-C.F.	Yes	59/Female	1/9/2013	38.09kg/m2	37.73kg/m2	7.6	9.7
26-W.M.	Yes	60/Female	10/31/2012	32.12kg/m2	32.12kg/m2	8.1	7.2
27-A.L.	Yes	62/Female	11/5/2012	31.64kg/m2	32.42kg/m2	9.2	8.9
28-R.R.	Yes	33/Male	8/21/2012	31.06kg/m2	31.33kg/m2	7.6	7.6
29-H.H.	Yes	70/Male	3/19/2012	38.74kg/m2	38.6kg/m2	8.9	7
30-D.L.	Yes	62/Male	2/14/2013	29.95kg/m2	29.79kg/m2	6.9	6.7
31-J.M.	Yes	70/Male	10/16/2012	31.53kg/m2	30.89kg/m2	6.2	5.5
32-V.B.	Yes	54/Male	11/2/2012	36.93kg/m2	36.48kg/m2	7.4	7.2
33-H.R.	Yes	43/Female	10/4/2012	31.41kg/m2	31.41kg/m2	8.4	8
34-F.B.	Yes	53/Male	11/2/2012	40.02kg/m2	39.82kg/m2	7.6	7.9
35-S.G.	Yes	56/Female	2/26/2013	39.89kg/m2	38.12kg/m2	8.8	8.6

Appendix C

Acceptance letter from Dr. Segal at Northeast Florida Endocrine and Diabetes Associates, P.A.

August 10, 2013

Scott A. Segel, M.D., F.A.C.E.
Northeast Florida Endocrine and Diabetes Associates, P.A.
3550 University Blvd. Suite 301
Jacksonville, Florida 32216
Phone #: (904) 384-2240

Dear University of North Florida Institutional Review Board,
I am granting permission to Katie Fetter, RN, BSN, (University of North Florida-Family Nurse Practitioner student), to complete her research study at my medical practice. I understand that her research study, *Efficacy of Bydureon in Type 2 Diabetic Patients*, must first be approved by the University of North Florida IRB. Ms. Fetter will have access to patients and to their clinical data for her retrospective chart review. Informed consent is not needed for this study. Please do not hesitate to contact me if you have any questions or concerns.

Sincerely,

Scott A. Segel, M.D., F.A.C.E.

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