Original Research

Glycemic Control Outcomes After Canagliflozin Initiation: Observations in a Medicare and Commercial Managed Care Population in Clinical Practice

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ABSTRACT

Purpose: Although the efficacy of canagliflozin has been well established in clinical trials, research regarding its use and impact on outcomes in clinical practice has been limited by the availability of data on observations up to and beyond 6 months after the initial use of canagliflozin. The purpose of this study was to evaluate changes in glycemic control after the initiation of canagliflozin use in a managed care population.

Methods: A retrospective cohort analysis in adults with type 2 diabetes mellitus was conducted using medical and pharmacy claims data and laboratory results from the Humana Research Database. The differences between hemoglobin (Hb) A_{1c} levels pre- and postindex were assessed. Changes from pre- to postindex in the percentages of patients achieving glycemic control (eg, HbA_{1c} <7% or <8%) were evaluated. HbA_{1c} levels were also observed during days 31 to 90, 91 to 180, 181 to 270, and 271 to 360 postindex relative to preindex to assess the durability of HbA_{1c} change over time. Analyses were conducted in the full cohort and in 3 subgroups: (1) HbA_{1c} ≥7% at baseline; (2) age ≥65 years; (3) and Medicare members age ≥65 years and HbA_{1c} ≥7% at baseline.

Findings: Among the 1562 patients meeting the study criteria, the mean HbA_{1c} values pre- and postindex were 8.6% and 7.9%, respectively ($P < 0.0001$); in the subgroup with HbA_{1c} ≥7% at baseline, these values were 8.9% and 8.0%; in the subgroup aged ≥65 years, 8.5% and 7.9%; and in the subgroup aged ≥65 years with HbA_{1c} ≥7% at baseline, 8.8% and 8.1% (all subgroups, $P < 0.001$). The percentages of patients meeting glycemic-control thresholds (HbA_{1c} <7%, <8%) were significantly greater at postindex in the full study cohort and in all 3 subgroups (all, $P < 0.001$). Based on longitudinal HbA_{1c} results in the postindex periods, HbA_{1c} reduction appeared durable across 12 months.

Implications: The findings from this study suggest that treatment with canagliflozin is associated with improved glycemic control, as evidenced by HbA_{1c} reduction and glycemic goal attainment. Even though not all patients had valid HbA_{1c} measurements available in each quarter during the follow-up period, the reductions in mean HbA_{1c} appeared durable across the postindex intervals. The observations from this majority Medicare Advantage with Prescription Drug sample and, more specifically, in the subgroups limited to patients aged ≥65 years are particularly informative for payers and providers managing or caring for patients of this age with diabetes. (*Clin Ther.* 2016;38:2046–2059)

Key words: canagliflozin, diabetes, glycemic control, HbA_{1c}, Medicare, SGLT2 inhibitors.

*The data from this article were previously published in abstract format: Bailey RA, Schwab P, Xu Y, Renda A, Pasquale M. A_{1c} change in canagliflozin users in a majority Medicare managed care population. Presented at: American Diabetes Association's 76th Scientific Sessions in Diabetes, New Orleans, La, June 10–14, 2016. Diabetes 2016;65(suppl 1):Abstract 2272.

Accepted for publication July 13, 2016.
http://dx.doi.org/10.1016/j.clinthera.2016.07.009
0149-2918/$ - see front matter

INTRODUCTION

Diabetes is one of the leading causes of morbidity and mortality in the United States.[1] In fact, 29.1 million Americans were reported to have diabetes in 2012, which amounted to 9.3% of the US population, and the total cost of diabetes in the United States in 2012 was US $245 billion.[2] The largest components of medical expenditures were hospital inpatient care (43% of the total medical cost) followed by prescription medications used to treat the complications of diabetes (18%).[2] In adults, type 2 diabetes mellitus (T2DM) accounts for ~90% to 95% of all diagnosed cases of diabetes.[1]

The risk for complications in T2DM is related to glycemic control, as measured by hemoglobin (Hb) A_{1c}, which remains a major focus of T2DM therapy. Several prospective, randomized trials have reported that lower HbA_{1c} levels are related to reduced rates of microvascular complications (eg, nephropathy, retinopathy, neuropathy) in T2DM patients.[3,4] Current treatment guidelines published jointly by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommend lowering HbA_{1c} to 7.0% in most patients, which should be considered within the context of an individual patient's needs, preferences, and tolerance levels.[5] Although the percentage of patients meeting their recommended goal for diabetes care increased by 8% from 1999 through 2010, almost half of US adults with diabetes did not meet the targets for glycemic control in 2010.[6]

Due to the clinical importance of glycemic control, health plan performance is partially evaluated based on the percentage of a plan's members with diabetes achieving glycemic control. The Healthcare Effectiveness Data and Information Set is a tool used to measure health plan performance that includes HbA_{1c} as part of the Comprehensive Diabetes Care measure.[7] Specifically, the percentage of a plan's members aged 18 to 75 years with diabetes who achieve glycemic control (HbA_{1c} <8%) is reported, as is the percentage with poor control (HbA_{1c} >9%). Additionally, the percentage of a select population of members achieving HbA_{1c} <7% is reported in the Healthcare Effectiveness Data and Information Set.[7] Medicare Advantage health plans may also receive bonus payments under the Centers for Medicare and Medicaid Services Star Ratings program for having a lower percentage of members with poor control (HbA_{1c} >9%) than their peers.[8]

As an adjunct to diet and exercise, multiple classes of antihyperglycemic agents (AHAs) are available to improve glycemic control in adults with T2DM. Canagliflozin is a sodium glucose cotransporter (SGLT)-2 inhibitor that was approved by the US Food and Drug Administration for the treatment of T2DM in March 2013.[9] SGLT2 inhibitors lower blood glucose by decreasing the reabsorption of filtered glucose in the kidneys, thereby increasing glucose excretion in urine. Several clinical trials conducted in adults with T2DM have provided evidence of increased tolerability and efficacy of canagliflozin compared with placebo and other AHAs in improving glycemic control.[10–16] In addition to improving glycemic control, canagliflozin was reported to decrease systolic blood pressure and weight in those studies, which is noteworthy given that some currently available oral antidiabetic drugs may cause weight gain. These findings are consistent in elderly patients with T2DM, although the HbA_{1c} reduction is slightly less in this group compared with that in younger adults.[17–19] This finding is reasonable given that the efficacy of canagliflozin depends on renal function and that older adults typically have a greater prevalence of a lower glomerular filtration rate, which represents decreased renal function.[20,21]

Although the efficacy of canagliflozin has been well established in clinical trials, research regarding its use and impact on outcomes in clinical practice is limited. Buysman et al[22] used data from a large US health plan of commercial and Medicare Advantage enrollees and found that the mean HbA_{1c} in adults with T2DM decreased significantly, from 8.54% to 7.76% ($P < 0.001$), within the first 3 months (mean, 67 days) after the initiation of canagliflozin use, but the follow-up time for HbA_{1c} observations was limited. In a recent study, Meckley et al[23] corroborated the finding of HbA_{1c} reduction with the use of canagliflozin using data from national commercial, Medicare, and Medicaid health plans. That study additionally reported results from a subgroup analysis conducted in elderly patients (age, ≥65 years), which found that the decrease in HbA_{1c} of 0.6% was significant ($P < 0.001$), but that the results need to be interpreted with caution due to the small sample size of the subgroup (39 patients).

Considering the existing evidence from clinical practice regarding canagliflozin utilization and outcomes in patients with T2DM, the primary objectives of the present study were to add to the existing evidence base