Diabetes-Related Composite Quality End Point Attainment: Canagliflozin Versus Sitagliptin Based on a Pooled Analysis of 2 Clinical Trials

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ABSTRACT

Purpose: This post hoc analysis evaluated attainment of diabetes-related composite quality measures (CQMs) with canagliflozin 100 mg, canagliflozin 300 mg, and sitagliptin 100 mg in patients with type 2 diabetes mellitus (T2DM). We used pooled data from two 52-week Phase III clinical trials evaluating the efficacy of canagliflozin 100 mg, canagliflozin 300 mg, and sitagliptin 100 mg.

Methods: CQMs assessed included the combined attainment of glycosylated hemoglobin (HbA_{1c}), blood pressure (BP), and LDL-C. To assess on-treatment differences at 52 weeks, odds ratios (ORs) and associated 95% CIs were calculated based on a logistic regression model. CQM attainment was assessed in the overall population and for patients with a body mass index $\geq$25 kg/m^2 at baseline.

Findings: Overall, baseline demographic and disease characteristics were comparable across treatment groups. Proportions of patients with T2DM meeting the CQMs HbA_{1c} <7.0%, BP <130/80 mm Hg, and LDL-C <100 mg/dL and HbA_{1c} <8.0%, BP <140/90 mm Hg, and LDL-C <100 mg/dL were similar at baseline. After 52 weeks of treatment, the proportion of patients meeting both CQMs was similar for canagliflozin 100 mg and sitagliptin 100 mg, and favored canagliflozin 300 mg versus sitagliptin 100 mg. For canagliflozin 300 mg, the OR was 1.79 (95% CI, 1.25–2.58) for the CQM HbA_{1c} <7.0%, BP <130/80 mm Hg, and LDL-C <100 mg/dL; the OR was 1.49 (95% CI, 1.15–1.92) for the CQM HbA_{1c} <8.0%, BP <140/90 mm Hg, and LDL-C <100 mg/dL. CQM attainments for patients with a body mass index $\geq$25 kg/m^2 were similar to those for the overall population.

Implications: At 52 weeks of treatment, this analysis observed comparable CQM attainment for canagliflozin 100 mg, and superior CQM attainment for canagliflozin 300 mg, compared with sitagliptin 100 mg. ClinicalTrials.gov identifiers are NCT01106677 and NCT01137812. (*Clin Ther.* 2015;37:1045–1054)

Key words: canagliflozin, composite quality measures, diabetes, quality measures, sitagliptin, T2DM.

INTRODUCTION

Diabetes is a chronic condition that can lead to complications, including retinopathy, nephropathy, neuropathy, and cardiovascular disease (CVD). Based on the complexity of diabetes, and its close association with these complications, the American Diabetes Association (ADA) recommends a multifactorial management approach that involves risk reduction strategies beyond glycemic control.[1] This approach includes control of blood pressure (BP) and lipids, in addition to glycemic control, to decrease the risks of CVD and nephropathy in this population.

The ADA currently recommends glycemic control to attain a glycosylated hemoglobin (HbA_{1c}) value of <7.0% in most adults with diabetes.[1] In addition, the ADA-recommended goals for BP management include a systolic BP (SBP) of <140 mm Hg in patients with diabetes (<130 mm Hg in patients for whom the benefits may outweigh the risks of stricter BP control)

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and <80 mm Hg for diastolic BP (DBP). The target for lipid control in patients with diabetes without overt CVD is a LDL-C value of <100 mg/dL, with an optional target of <70 mg/dL for diabetes patients with CVD. Current evidence suggests that attainment of these recommended goals remains suboptimal, with only slightly more than one half of all subjects with diabetes in the United States meeting each of these individual clinical goals for treatment.[2,3]

The high burden of diabetes is associated with high costs of health care for those with the disease; a majority of these costs are associated with the complications of diabetes.[4] Due to these high costs, diabetes has been the focus of performance measurements, quality improvement initiatives, and, more recently, pay-for-performance programs.[5] Most of these initiatives have focused on attainment of individual quality measures (QMs), including HbA_{1c}, BP, and LDL-C. In an effort to further improve care of patients with diabetes, there is a movement away from tracking performance on separate measures and instead using composite QMs (CQMs), which are used to determine whether all crucial aspects of care have been achieved for an individual patient. CQMs are used to assess the care of patients with a given condition, such as diabetes, with the goal of determining whether comprehensive evidence-based care is being provided. For diabetes, CQMs assess the combined attainment of glycemic control, BP control, and lipid control. The ultimate goal of the use of CQMs is to allow for measurement across clinicians and to encourage coordination of care across multiple health care professionals and settings of care.[6]

CQMs are used in several communities for public reporting and quality improvement programs.[7] These community programs include the MN Community Measurement, the Wisconsin Collaborative for Healthcare Quality, and the Health Collaborative of Greater Cincinnati, all of which include diabetes CQMs (**Table I**). Diabetes-focused CQMs are also currently included as a metric in Medicare's Accountable Care Organization programs.[8] The attainment of diabetes-related CQMs in the United States is lower than that for individual QMs, with <20% of patients with diabetes attaining the combined target goals of HbA_{1c} <7.0%, BP <130/80 mm Hg, and LDL-C <100 mg/dL in 2007 through 2010.[2]

Antihyperglycemic agents (AHAs) are used to manage diabetes as an adjunct to diet and exercise to improve glycemic control. The clinical attributes of available AHAs differ and, as a result, may differentially impact CQMs. Canagliflozin is a sodium-glucose cotransporter 2 inhibitor, and sitagliptin is a dipeptidyl peptidase-4 inhibitor; both are approved for use as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM).[9,10] Two 52-week, Phase III clinical trials have compared the efficacy and safety of canagliflozin and sitagliptin in patients with T2DM.[11,12] In patients with T2DM who had inadequate glycemic control on metformin, HbA_{1c} reductions were similar with canagliflozin 100 mg, and were statistically superior with canagliflozin 300 mg, compared with sitagliptin at 52 weeks.[11] In addition, both canagliflozin doses demonstrated significantly greater reductions in weight and SBP versus sitagliptin 100 mg. In patients with T2DM who had inadequate glycemic control with metformin and a sulfonylurea, canagliflozin 300 mg demonstrated statistically superior glycemic control and significantly greater reductions in SBP and weight compared with sitagliptin 100 mg.[12]

Because CQMs are used in various quality improvement, public reporting, and pay-for-performance programs, the comparative performance of available AHAs on CQMs may be of interest to payers and clinicians when making formulary and treatment decisions. A previous study evaluated the comparative CQM attainment of canagliflozin 300 mg versus sitagliptin 100 mg in patients with T2DM previously treated with metformin plus a sulfonylurea at baseline (based on a post hoc analysis of the study by Schernthaner et al).[12] This evaluation reported better attainment of CQMs with canagliflozin 300 mg compared with sitagliptin 100 mg.[13] Because payers and health care professionals are likely to see a T2DM population across the spectrum of background AHA treatment, the present analysis was undertaken to evaluate patients' baseline treatment with either metformin alone or metformin plus a sulfonylurea, and to address the increasing need for information regarding the impact of AHAs on CQMs. Because patients classified as overweight/obese comprise a large proportion of the T2DM population, have associated higher health care costs, and are the focus of some QM programs, assessing CQM attainment in the overweight/obese population is also of interest.[14–16] The objective of this post hoc analysis from 2 active comparator trials was to assess and compare