Impact of SGLT2 Inhibitors (SGLT2i) on Cardiovascular (CV) Risk and Estimated Glomerular Filtration Rate (eGFR) in the EXSCEL Placebo Group

LINDSAY CLEGG, HIDDO L. HEERSPINK, ROBERT C. PENLAND, WEIFENG TANG, DAVID W. BOULTON, SRINIVAS BACHINA, ROBERT D. FOX, PETER FENICI, MARCUS THURESSON, ROBERT J. MENTZ, ADRIAN F. HERNANDEZ, M. ANGELYN BETHEL, and RURY R. HOLMAN

Abstract

SGLT2i, empagliflozin and canagliflozin, have been shown to reduce the incidence of major adverse CV events (MACE), all-cause mortality (ACM) and renal events in CV outcomes trials (CVOTs), with robust real-world evidence (RWE) suggesting class effect benefits. In the exenatide CVOT EXSCEL, ~10% of patients took an SGLT2i with ~5% use of dapagliflozin (DAPA). Effects of all SGLT2i, and DAPA alone, on MACE, ACM, and eGFR were analyzed in EXSCEL participants randomized to placebo.
were generated, based on their last measured characteristics before SGLT2i initiation. Subsequent time-to-first adjudicated MACE and ACM were compared using a Cox regression. Decline in eGFR over time (slope) was quantified in the matched cohorts using a mixed model repeated measurement (MMRM) analysis.

SGLT2i overall, and DAPA alone, numerically decreased the MACE hazard ratio, and SGLT2i significantly reduced the ACM risk (Table). The eGFR slope was improved significantly for SGLT2i overall and DAPA alone (Table).

This post-hoc EXSCEL analysis supports a beneficial class effect for SGLT2i on MACE, ACM, and renal function, consistent with published CVOTs, Real-World data, and for DAPA alone. DECLARE, the ongoing DAPA CVOT, will complete in 2018.

**Disclosure**
- **L. Clegg**: Employee; Self; AstraZeneca.
- **H.L. Heerspink**: Consultant; Self; AbbVie Inc., AstraZeneca. Advisory Panel; Self; Boehringer Ingelheim GmbH. Consultant; Self; Janssen Research & Development, Fresenius SE & Co. KGaA. Advisory Panel; Self; Merck & Co., Inc.. Consultant; Self; Mitsubishi Tanabe Pharma Corporation. **R.C. Penland**: Employee; Self; AstraZeneca.
- **W. Tang**: Employee; Self; AstraZeneca.
- **D.W. Boulton**: Employee; Self; AstraZeneca. Stock/Shareholder; Self; Novartis Pharmaceuticals Corporation. **S. Bachina**: Employee; Self; AstraZeneca.
- **R.D. Fox**: None. **P. Fenici**: Employee; Self; AstraZeneca. **M. Thuresson**: Consultant; Self; AstraZeneca. **R.J. Mentz**: Research Support; Self; AstraZeneca, GlaxoSmithKline plc., Merck & Co., Inc.
- **A.F. Hernandez**: Research Support; Self; AstraZeneca, GlaxoSmithKline plc., Merck & Co., Inc.
Renal Outcomes in the EXenatide Study of Cardiovascular Event Lowering (EXSCEL)
YULIYA LOKHNYGINA et al., Diabetes, 2018

Lower Risk of CV Events and Death Associated with Initiation of SGLT2 vs. DPP-4 Inhibitors—Analysis from the CVD-REAL 2 Study
MARCUS THURESSON et al., Diabetes, 2018

Cardiovascular Event Hazards over Time in TECOS
M. ANGELYN BETHEL et al., Diabetes, 2018

EXSCEL—Once-Weekly Exenatide Reduces Medical Resource Utilization in

We recommend

ASCO: Complete Lymph Node Dissection Does Not Improve Survival in Patients With Melanoma and Micrometastases
Univadis (UK), 2015

Cancer Risk From Diabetes Drugs Unproven, Say AACE/ACE
Miriam E. Tucker et al., Medscape

Potential modification of the UKPDS risk engine and evaluation of macrovascular event rates in controlled clinical trials
Fred Yang et al., Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 2013