A Closer Look at the Endocrine and Metabolism PRN

Overview of the PRN

Endocrine and Metabolism (E & M) PRN members practice in a variety of settings, including ambulatory care clinics, academia, community settings, and hospital settings. Areas of practice and research interests of members include diabetes, dyslipidemia, general primary care, and metabolic disorders. The PRN was formed to achieve the following goals and objectives:

1. Provide an opportunity for pharmacists with an interest in endocrine and metabolic disorders to promote practice, research, and education in these areas;
2. Provide a mechanism for members with similar interests to meet during ACCP meetings to network, problem solve, and discuss professional issues and opportunities; and
3. Promote practice involvement; educational needs of health care professionals, students, and patients; and research activities in endocrinology and metabolism that this ACCP PRN effort may favorably influence.

PRN Leadership:

Chair:
Michelle L. Rager, Pharm.D., BCPS, CDE
Chair-Elect:
Christie A. Schumacher, Pharm.D., BCPS, BCACP, BC-ADM, CDE
Secretary/Treasurer:
Rick Hess, Pharm.D., CDE, BC-ADM

Membership Overview:

Total Members: 368
Student Members: 106
Resident Members: 16
Fellow Members: 2

Opportunities and Resources for Student, Resident, and Fellow Members

The E & M PRN Trainee Travel Grant is intended to provide financial support for one or more students, residents, and/or fellows attending the ACCP Annual Meeting. Recipients of the travel grant are required to give a brief (10 minutes) presentation on an endocrine/metabolism topic at the E & M PRN business and networking meeting during the Annual Meeting. The presentation can be an endocrine- or metabolism-related clinical pearl, description of an ongoing or completed research project, or journal article review. Recipients of the travel grant will be assigned a mentor (who is an E & M PRN member) who can provide guidance in preparing this presentation. For the 2017 ACCP Annual Meeting, up to two $500 grants will be awarded: one to a pharmacy resident or fellow and one to a pharmacy student.

Residents and fellows are encouraged to participate in any of the following committees:

- **Education Committee:** Responsible for developing the PRN focus session at the ACCP Annual Meeting
- **Membership Committee:** Responsible for selecting recipients for the PRN trainee travel awards and engaging members in PRN activities
- **Communications Committee:** Responsible for overseeing and monitoring the PRN's e-mail list, webpage, and Facebook page and publishing PRN newsletters
- **Networking Committee:** Responsible for organizing PRN networking functions at national pharmacy meetings
- **Health Care Committee:** Responsible for keeping PRN members updated with new and emerging issues that affect pharmacists practicing in the endocrine and metabolism specialty
- **Research Committee:** Responsible for developing potential topics for PRN papers and publications as well as facilitating communication and collaboration with the ACCP Practice-Based Research Network (PBRN)

Clinical Issues: Cardiovascular Outcome Trials of Type 2 Diabetes

Studies have shown that lowering hemoglobin A1C reduces microvascular complications; however, cardiovascular (CV) results have been inconclusive.[1,2] A meta-analysis examining the safety of rosiglitazone showed an increased risk of myocardial infarction (OR 1.43; p=0.03) and a trend toward an increased risk from CV causes (OR 1.64; p=0.06).[3] These adverse findings associated with rosiglitazone led the U.S. Food and Drug Administration (FDA) to mandate that any new antidiabetes medication used in the treatment of type 2 diabetes show that it is not associated with an unacceptable increase in CV risk. The FDA stipulated that these new diabetes medications must undergo noninferiority studies with a preset margin of less than 1.3 and a primary outcome of the composite of CV death, nonfatal myocardial infarction, or nonfatal stroke. The FDA also requires that a minimum of 2 years of CV safety data be collected and that patients who have renal impairment, advanced age, and/or advanced disease be included.

Since this 2008 FDA mandate, six studies have been published on three dipeptidyl peptidase-4 (DPP-4) inhibitors, one sodium-glucose co-transporter-2 (SGLT-2) inhibitor, and two glucagon-like peptide-1 (GLP-1) receptor agonists. Each of the following studies is a randomized, double-blind, placebo-controlled, noninferiority trial that includes patients at high risk of CV disease. Table 1 describes the trials and the clinical findings of each.

Table 1. Summary of Recent CV Outcome Studies Involving Antidiabetes Medications

Drug Class	Trial	Primary End Point	Results (Drug vs. Placebo)	Considerations
DPP-4 inhibitors	TECOS[4] (sitagliptin)	MACE + unstable angina	n=14,671 Follow-up: 3 yr Primary outcome: 11.4% vs. 11.6% NI: p<0.001	• Sitagliptin showed CV safety with respect to CV death, MI, or ischemic stroke • No difference in HF hospitalizations
	SAVOR-TIMI 53[5] (saxagliptin)	MACE	n=16,492 Follow-up: 2.1 yr Primary outcome: 7.3% vs. 7.2% NI: p<0.001 S: p=0.99	• Saxagliptin was associated with an increase in HF hospitalizations (3.5% vs. 2.8%; HR 1.27; p=0.007) • This increased risk of HF hospitalizations was highest in the first year after patients started treatment ○ Patients with a history of HF, high baseline BNP concentrations, and CKD had increased risk
	EXAMINE[6] (alogliptin)	MACE	n=5380 Follow-up: 18 mo Primary outcome: 11.3% vs. 11.8% NI: p<0.001	• Hospitalizations for HF higher in the alogliptin group (106) than in placebo (89) • Rate 2.6 vs. 2.3 cases per 100 patient-years (HR 1.19) • Post hoc analysis of CV death and hospital admission for HF showed no difference in patients with a history of HF • Showed greater risk in patients without a history of HF in the alogliptin group (2.2% vs. 1.3%; HR 1.76; p=0.026)
SGLT-2 inhibitors	EMPA-REG[7] (empagliflozin)	MACE	n=7020 Follow-up: 3.1	• Death from CV causes drove the composite end point • Decrease in HF hospitalizations (2.7% vs. 4.1% – 35%

			yr Primary outcome: 10.5% vs. 12.1% S: HR 0.86 (95% CI, 0.74–0.99) p=0.04 NNT: 63	relative risk reduction) • Differences in HF hospitalizations, death from CV causes, and death from any cause occurred early in follow-up and were maintained to the end of follow-up
Drug Class	**Trial**	**Primary End Point**	**Results (Drug vs. Placebo)**	**Considerations**
GLP-1 agonists	LEADER[8] (liraglutide)	MACE	n=9340 Follow-up: 3.8 yr Primary outcome: 13% vs. 14.9% NI: p<0.001 S: HR 0.87 (95% CI, 0.78–0.97) p=0.01 NNT: 53	• Death from CV causes drove the primary composite end point • No difference in HF hospitalizations • Weight loss 2.3 kg greater in the liraglutide arm • Statistically significant reductions in nephropathy in the liraglutide arm compared with placebo • Increase in acute gallstone disease in the liraglutide arm with no differences in acute pancreatitis
	SUSTAIN-6[9] (semaglutide)	MACE	n=2735 Follow-up: 2.1 yr Primary outcome: 6.6% vs. 8.9% NI: p<0.001 S: HR 0.74 (95% CI, 0.58–0.95) p=0.02 NNT: 44	• Nonfatal stroke drove the primary composite outcome • No difference in HF hospitalizations • Increase in retinopathy complications in the semaglutide group • Mean weight loss was 3.6 and 4.9 kg in the low- and high-dose semaglutide groups, respectively

BNP = B-type natriuretic peptide; CI = confidence interval; CKD = chronic kidney disease; HF = heart failure; HR = hazard ratio; MACE = major adverse cardiovascular events; MI = myocardial infarction; NI = noninferiority; NNT = numbered needed to treat; S = superiority.

The 2016 American Diabetes Association (ADA) guidelines recommend metformin as first-line therapy. For combination therapy, the ADA guidelines do not specify which drug class should be added to metformin.[10] The American Association of Clinical Endocrinologists guidelines recommend adding a GLP-1 receptor agonist to metformin therapy.[11] Clinically, these studies do not guide our decision-making process at this time except in the use of DPP-4 inhibitors in patients with heart failure. How the guidelines will incorporate the findings of these CV outcome trials into their recommendations remains to be seen. For now, they will contribute to the approval process for bringing new diabetes medications to market. Cardiovascular outcome trials are being conducted for canagliflozin, dapagliflozin, exenatide, and linagliptin.

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Submitted by:
Kristin Bradley, Pharm.D., BCPS
Christie Schumacher, Pharm.D., BCPS, BCACP, BC-ADM, CDE
Michelle Rager, Pharm.D., BCPS, CDE
Rick Hess, Pharm.D., BC-ADM, CDE