Protein Kinase C-β (PKC-β) Inhibition: A Promise not yet Fulfilled

Ruboxistaurin, an oral PKC-β, was withdrawn on March 15, 2007 by Eli Lilly
Dual Inhibition of Classical Protein Kinase C-α and Protein Kinase C-β Isoforms Protects Against Diabetic Nephropathy
ASCEND Trial:
Endothelin Receptor Antagonist Avosentan
Significantly Decreased Albuminuria

Terminated due to increased CHF and deaths

Addition of Atrasentan, an Endothelin Receptor Antagonist, to RAS Blockade Reduces Albuminuria in Diabetic Nephropathy

Baseline UACR ~400 mg/g CR
Atrasentan Restores Endothelial Glycocalyx Thickness

Diabetes 2016;65:2429-2439
Pirfenidone, an Inhibitor of TGF-β at 1200 mg/d, but NOT 2400 mg/d, Improves eGFR from Baseline

Pirfenidone (Esbriet) approved to treat idiopathic pulmonary fibrosis

Pentoxifylline-Lower Decline in eGFR and Greater UAE Reduction

Baseline UAE ~1000 mg/day
CCX140-B (CCR2 Antagonist) Lowers Albuminuria in Patients with Type 2 DM

Monocyte chemoattractant protein-1 (MCP-1), also called C-C chemokine receptor 2 (CCR2)

Baseline UAE 400 mg/day

Lancet Diabetes & Endo 2015;3:687-696
Pyridoxamine (Pyridorin), a Derivative of Vitamin B6, Inhibits the Formation of Advanced Glycation Endproducts

I.V. form of Pyridorin for use in hospital-acquired acute kidney injury
Finerenone, a 3rd Generation Nonsteroidal Mineralocorticoid Receptor Antagonists Lowers Albuminuria

Baseline UACR ~200 mg/g CR

JAMA 2015;314:884-894
Patiromer (Veltassa)—
Twice Daily Lowered Potassium Levels

FDA Approved on October 22, 2015 but with a **Black Box Warning**
Sodium Zirconium Cyclosilicate (ZS-9) 3X Daily X2 days ↓ Hyperkalemia

AstraZeneca receives Complete Response Letter from FDA May 27, 2016

JAMA 2014;312:2223-2233
Metformin Improves Whole-Body Glycocalyx Barrier Properties