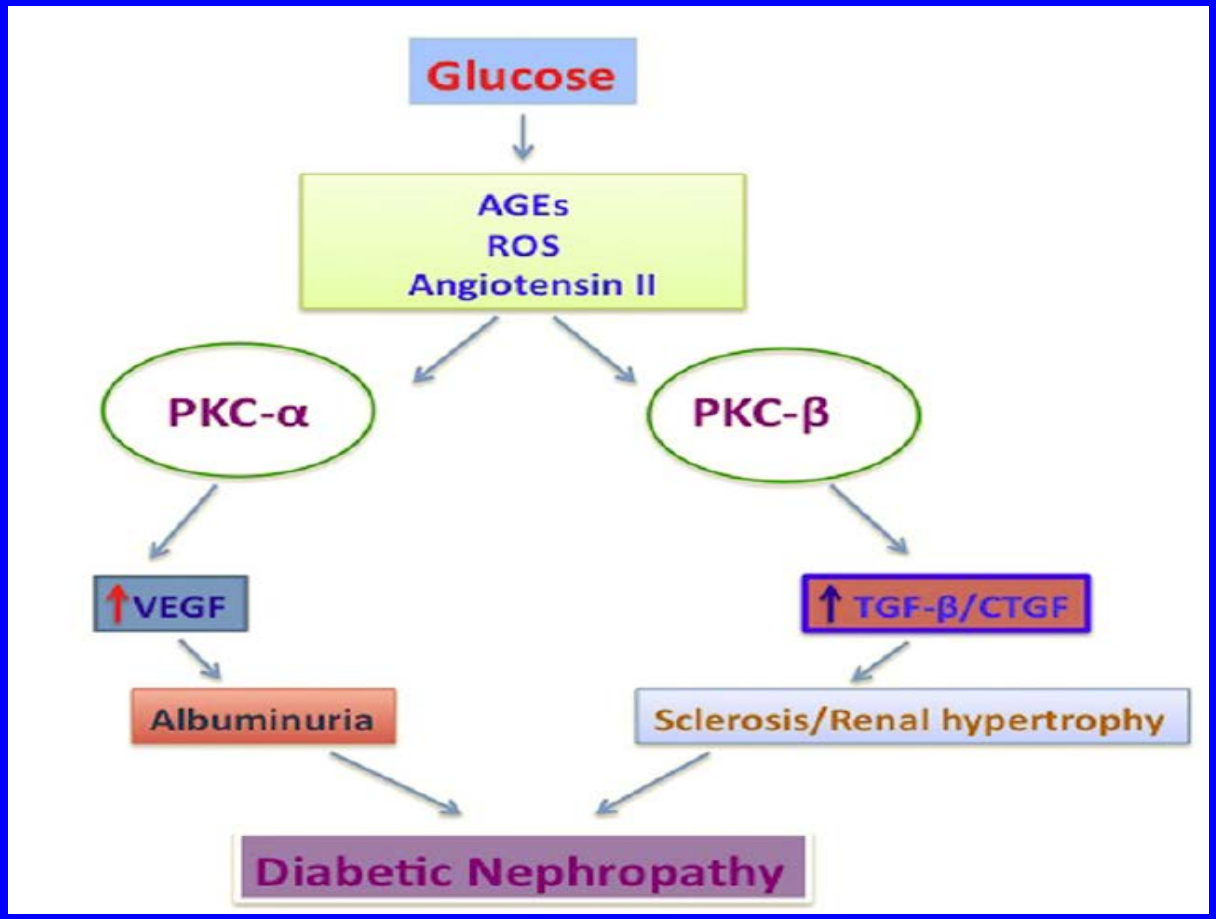
Protein Kinase C-β (PKC-β) Inhibition: A Promise not yet Fulfilled

Ruboxistaurin, an oral PKC-β, was withdrawn on March 15, 2007 by Eli Lilly



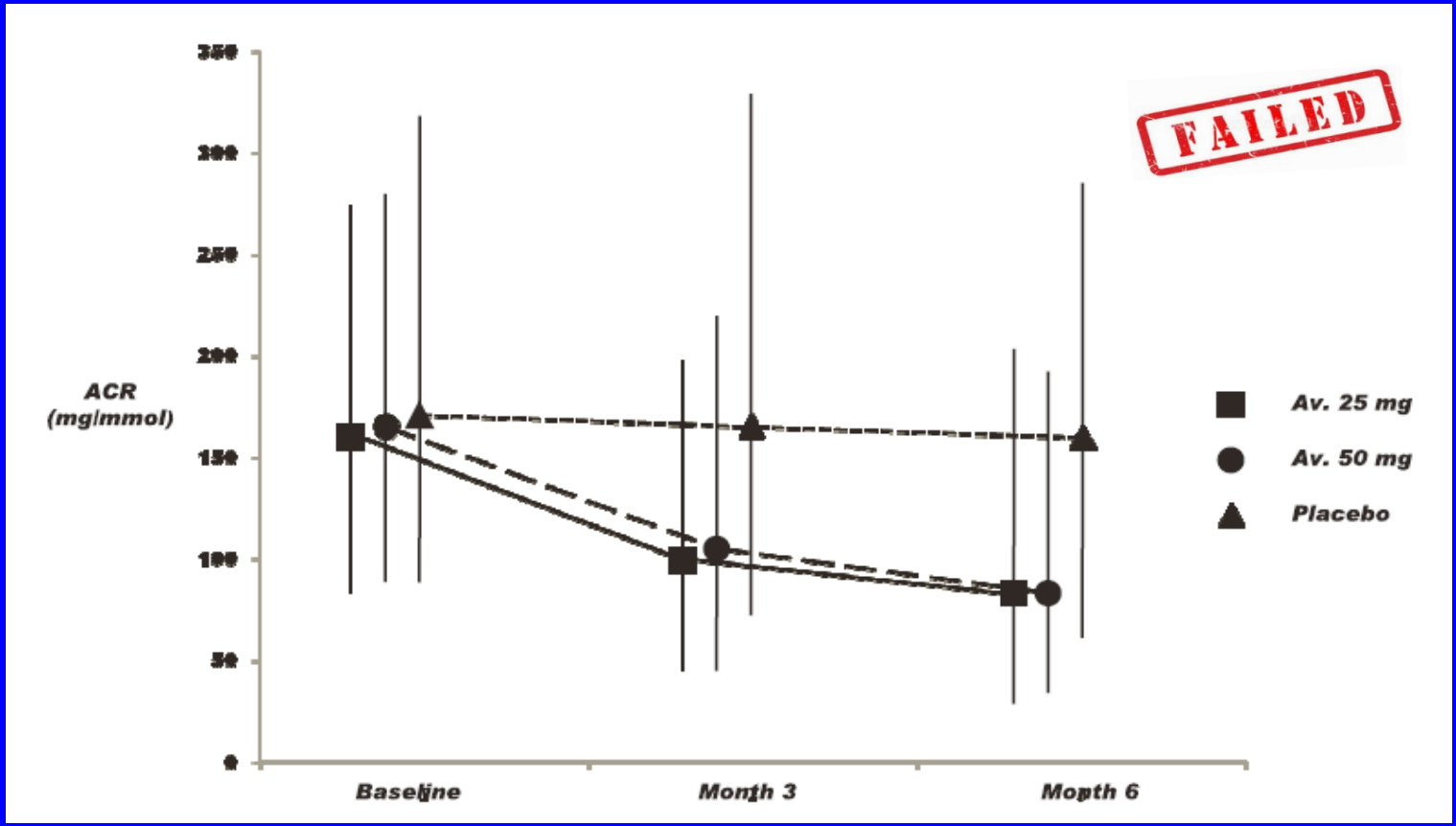
Dual Inhibition of Classical Protein Kinase C-α and Protein Kinase C-β Isoforms Protects Against Diabetic Nephropathy





Diabetes 2013;62:1010-1011

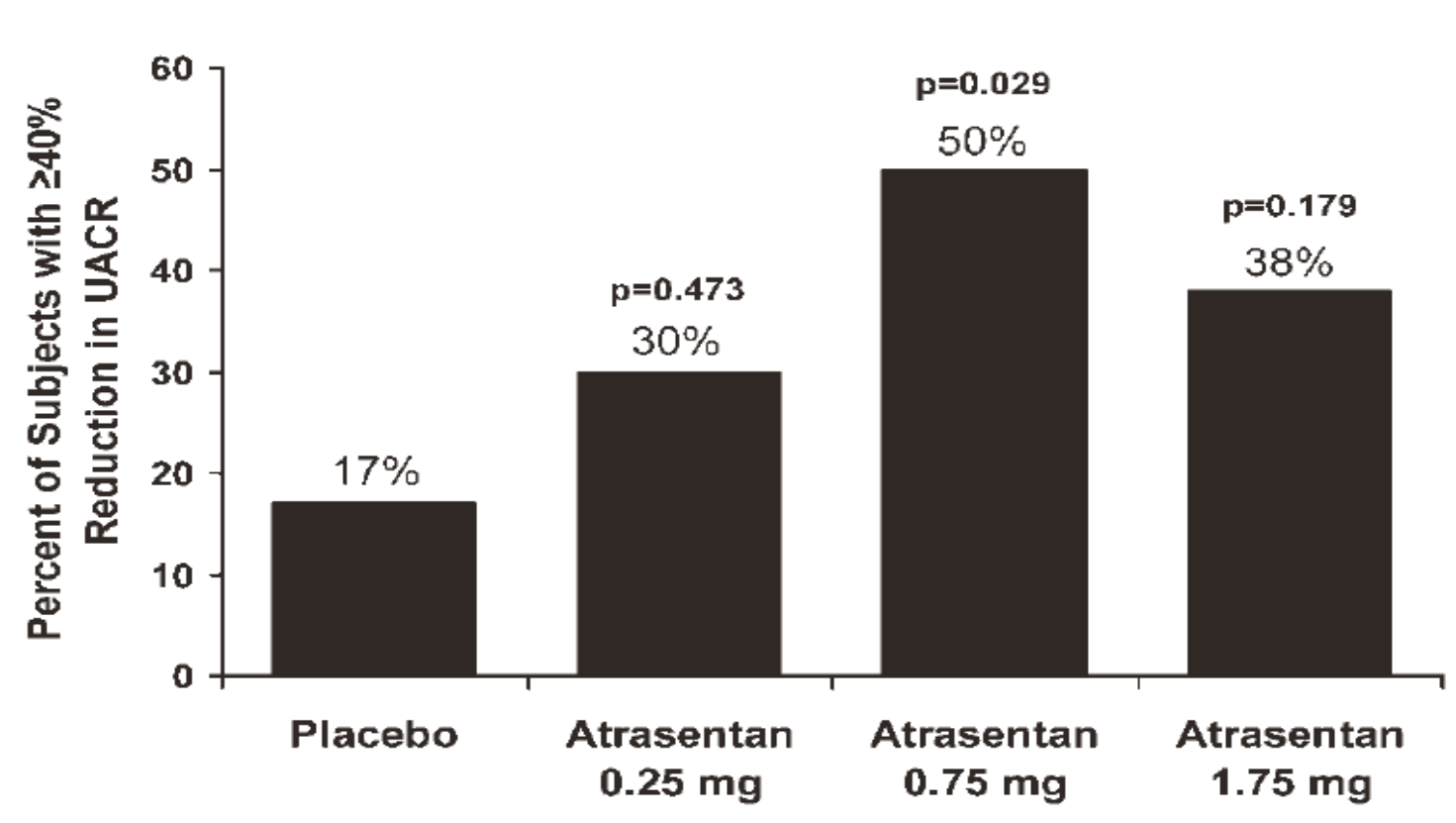
ASCEND Trial: Endothelin Receptor Antagonist Avosentan Significantly Decreased Albuminuria



Terminated due to increased CHF and deaths

J Am Soc Nephrol 2010;21:527–535

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

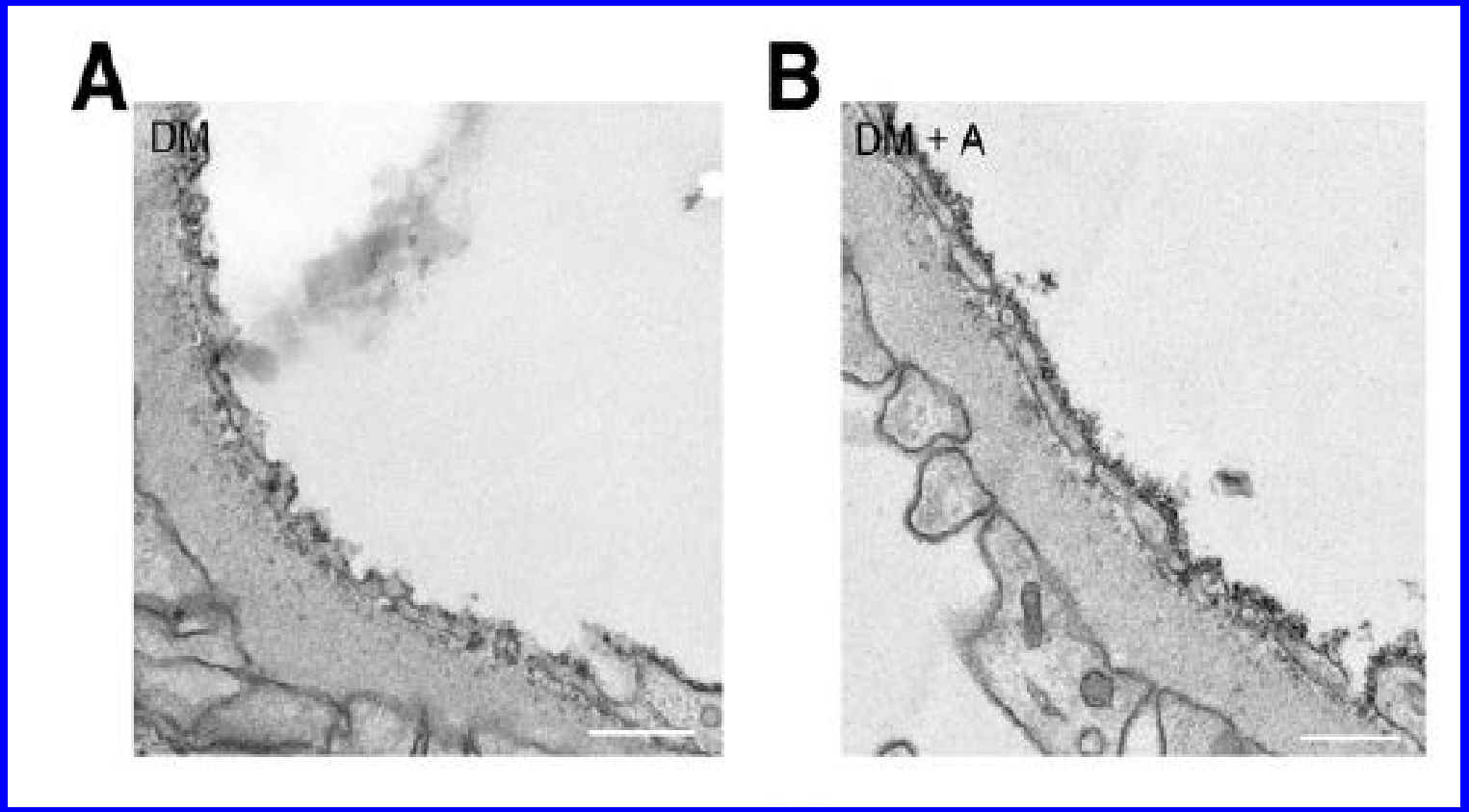


Baseline UACR ~400 mg/g CR



J Am Soc Nephrol 2011;22:763-772

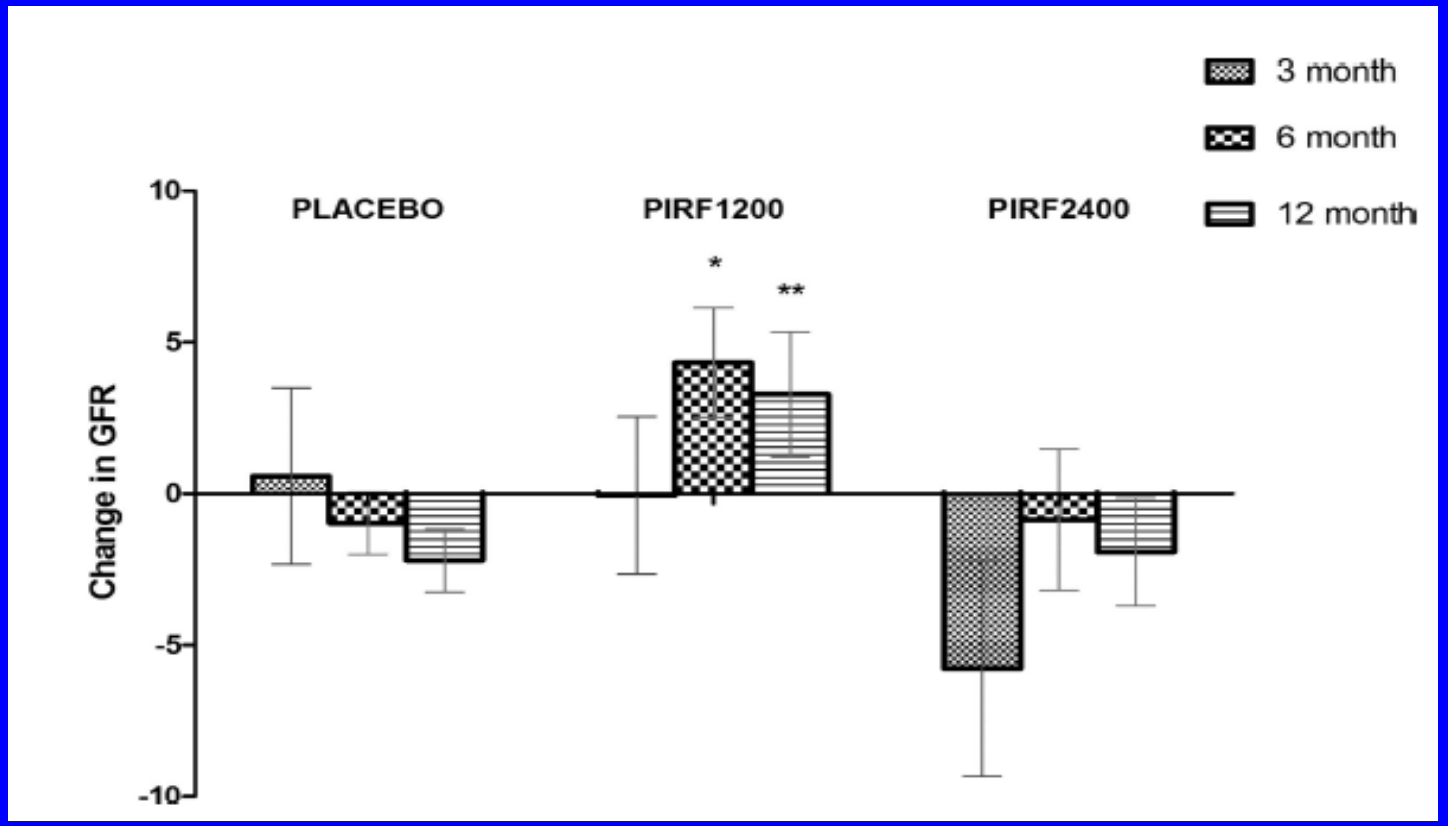
Atrasentan Restores Endothelial Glycocalyx Thickness





Diabetes 2016;65:2429-2439

Pirfenidone, an Inhibitor of TGF-β at 1200 mg/d, but NOT 2400 mg/d, Improves eGFR from Baseline

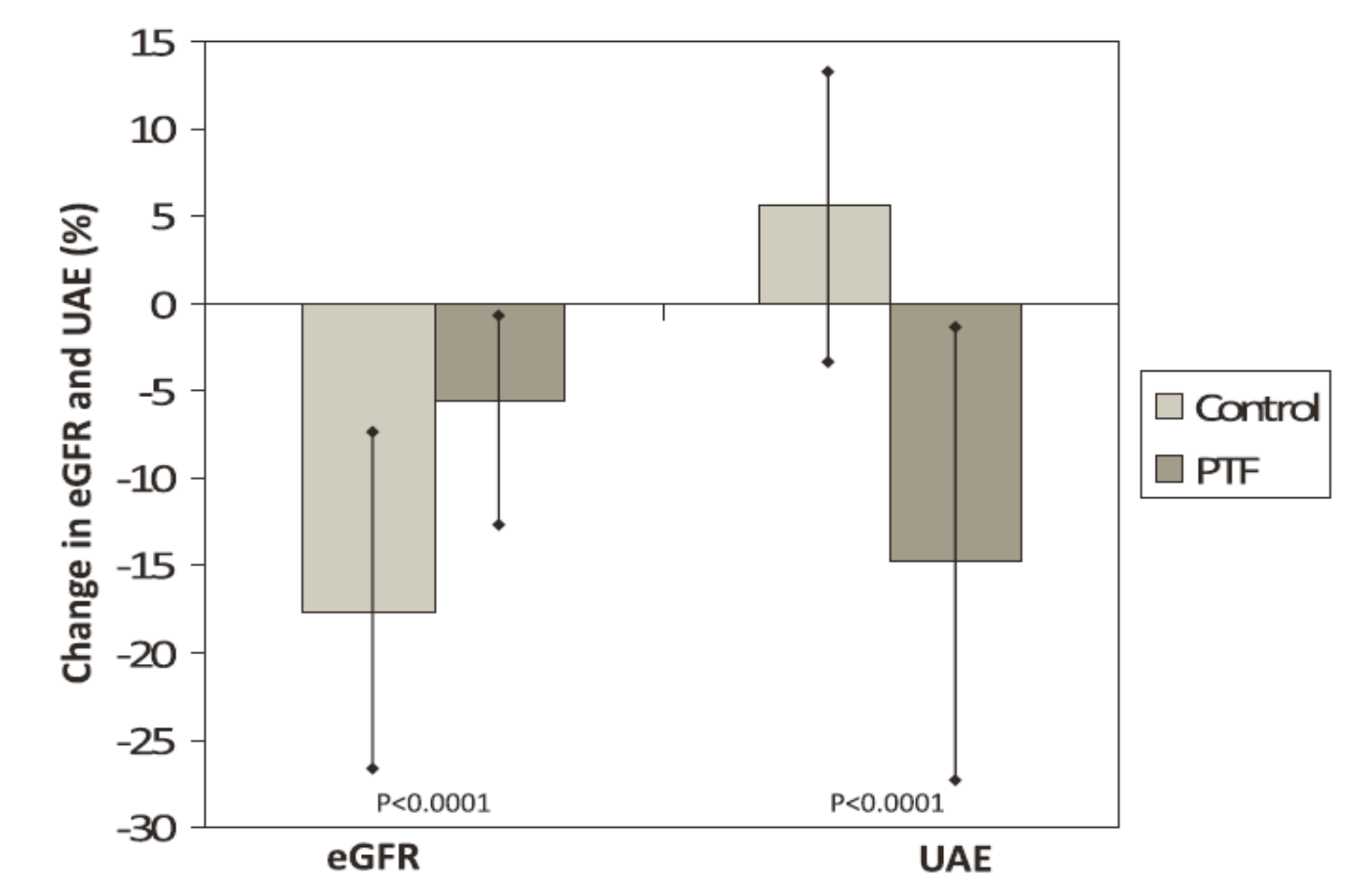




Pirfenidone (Esbriet) approved to treat idiopathic pulmonary fibrosis

J Am Soc Nephrol 2011;22:1144–1151

Pentoxifylline-Lower Decline in eGFR and Greater UAE Reduction



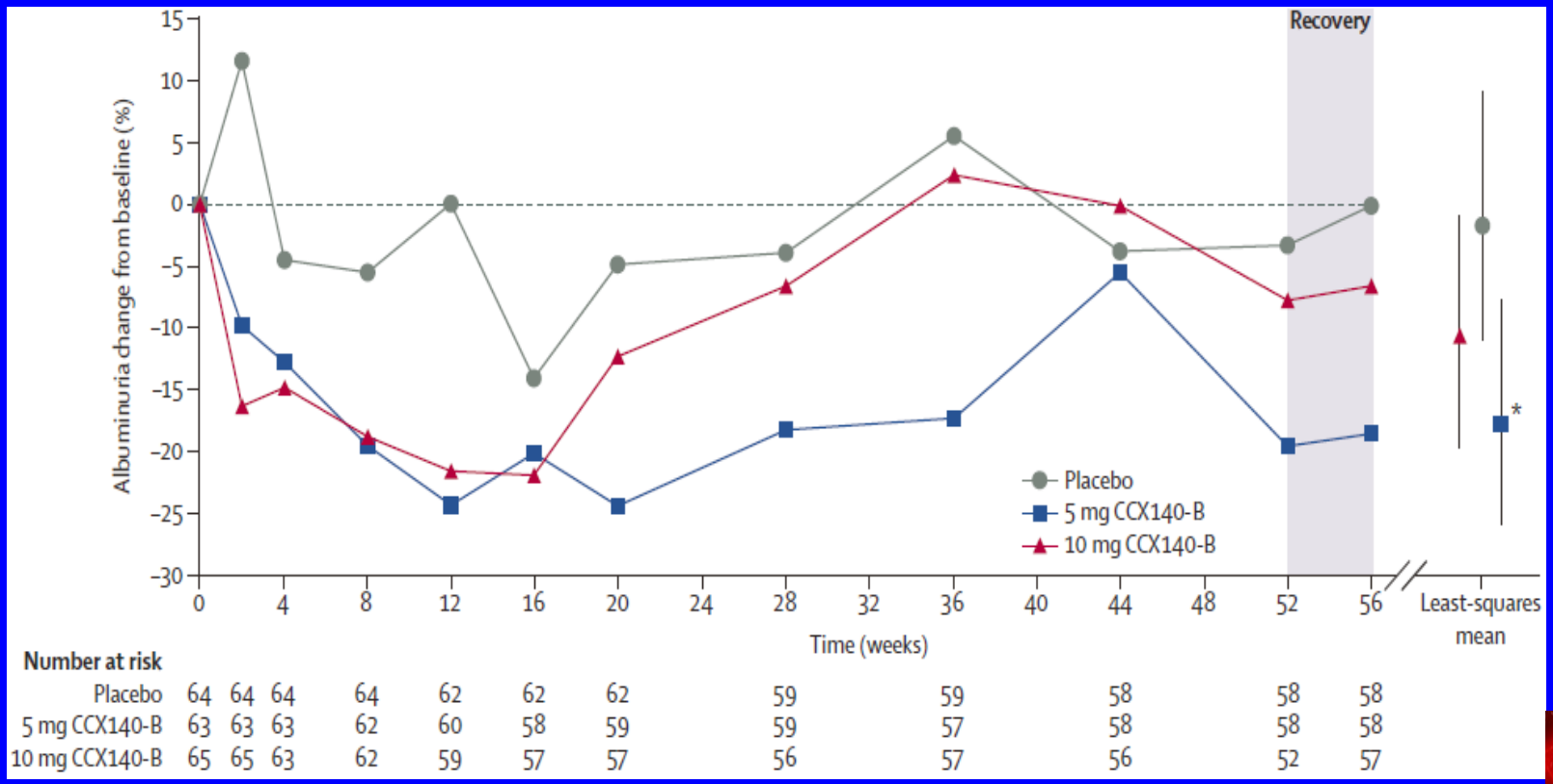
Baseline UAE ~1000 mg/day



J Am Soc Nephrol 2015;26:220–229

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)



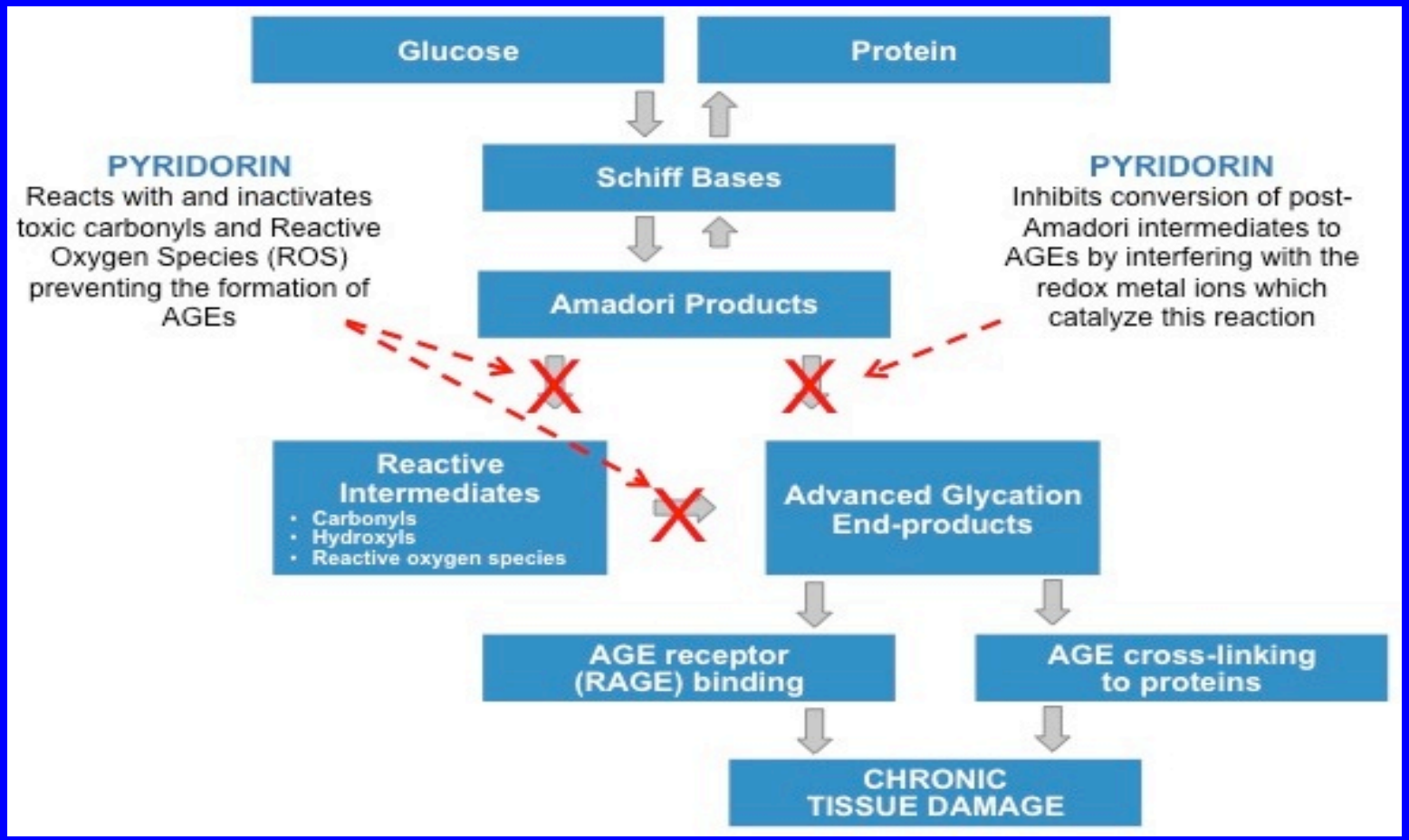
Baseline UAE 400 mg/day



Lancet Diabetes & Endo 2015;3:687-696

Pyridoxamine (Pyridorin), a Derivative of Vitamin B6, Inhibits the Formation of Advanced Glycation Endproducts

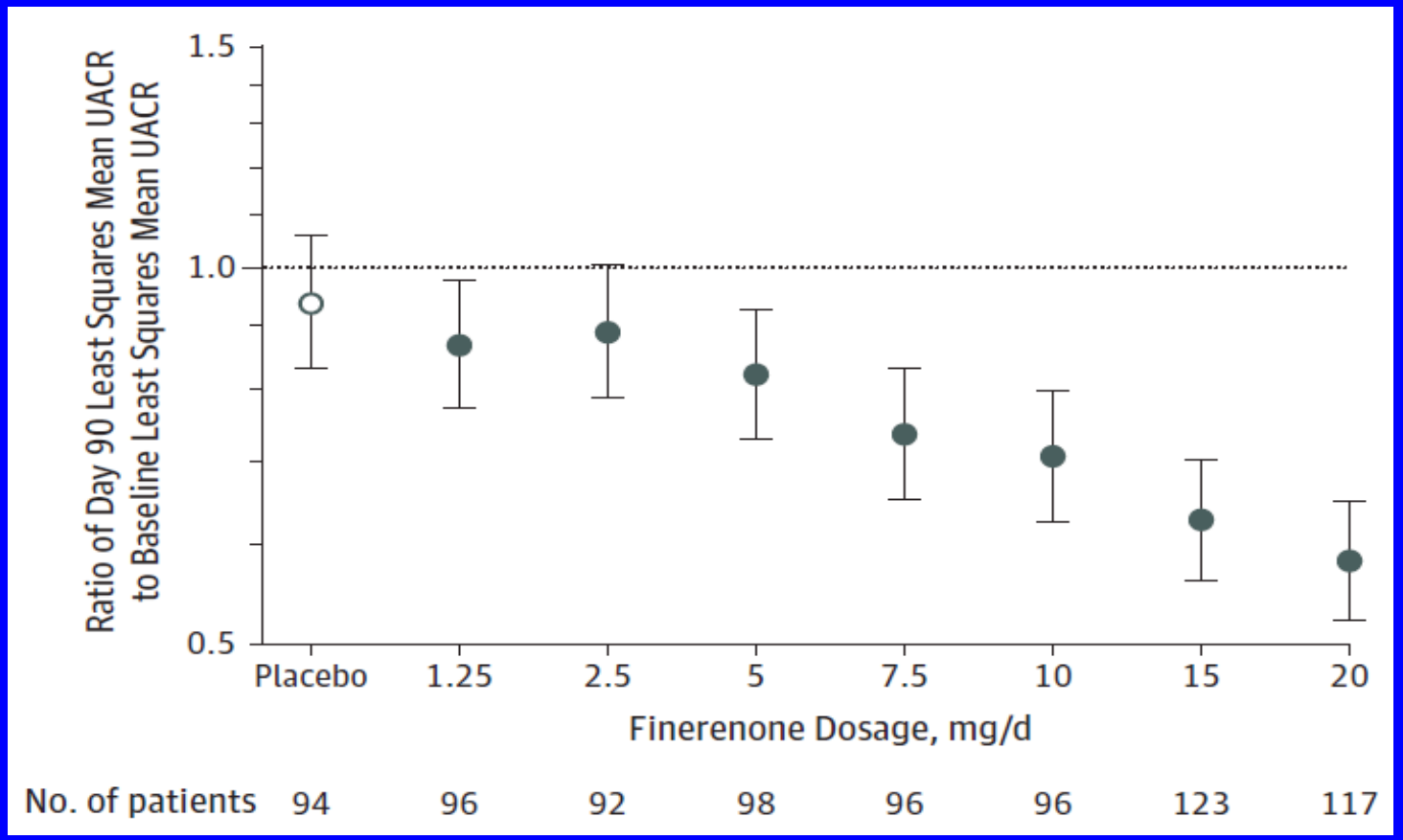
I.V. form of Pyridorin for use in hospital-acquired acute kidney injury



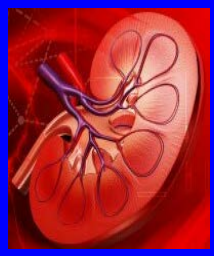


Nephron 2015;129:22–28

Finerenone, a 3rd Generation Nonsteroidal Mineralocorticoid Receptor Antagonists Lowers Albuminuria



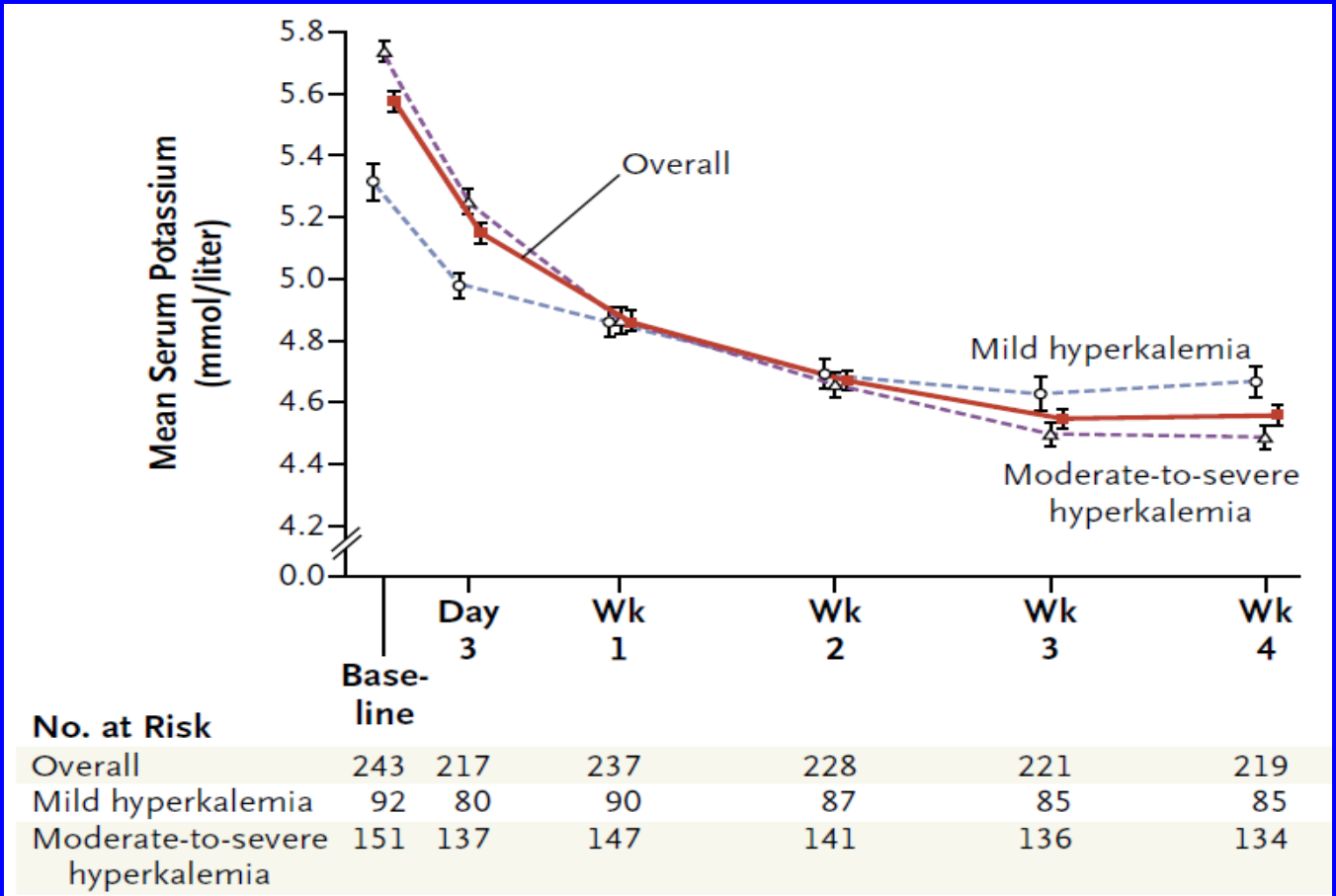
Baseline UACR ~200 mg/g CR



JAMA 2015;314:884-894

Patiromer (Veltassa)— Twice Daily Lowered Potassium Levels

FDA Approved on October 22, 2015 but with a Black Box Warning

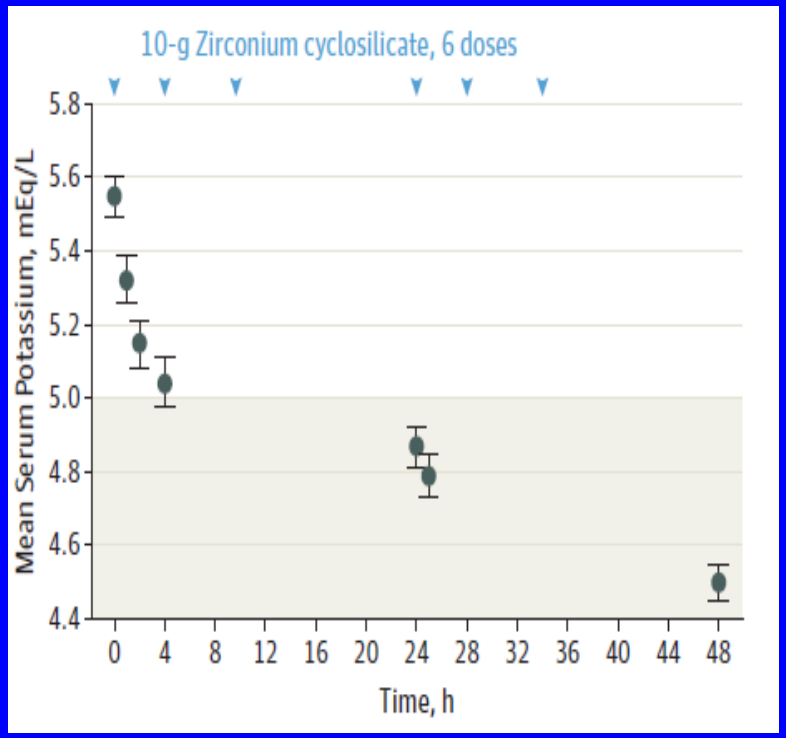


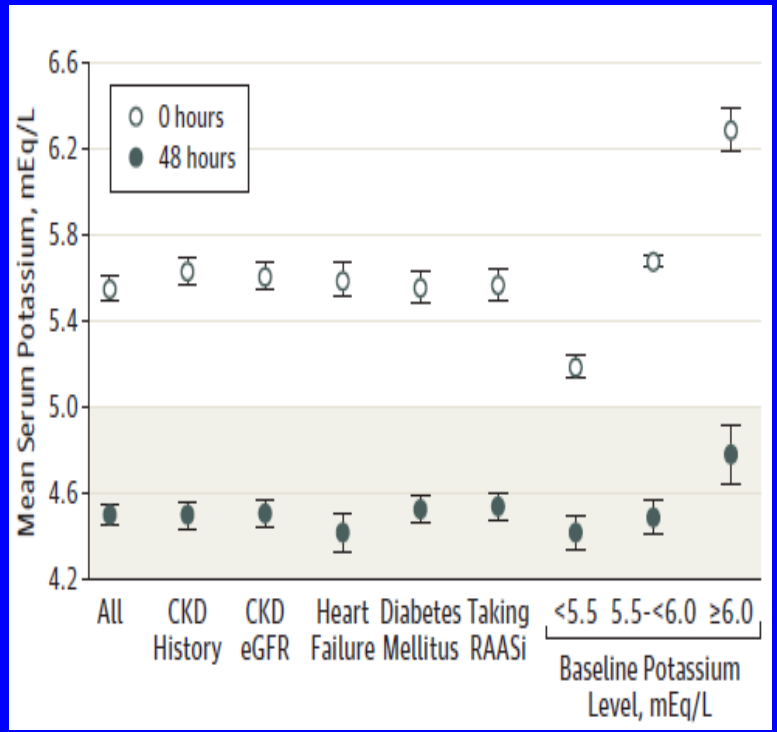
No. at Risk						
Overall	243	217	237	228	221	219
Mild hyperkalemia	92	80	90	87	85	85
Moderate-to-severe hyperkalemia	151	137	147	141	136	134

N Engl J Med 2015;372:211-221

Sodium Zirconium Cyclosilicate (ZS-9) 3X Daily X2 days ↓ Hyperkalemia

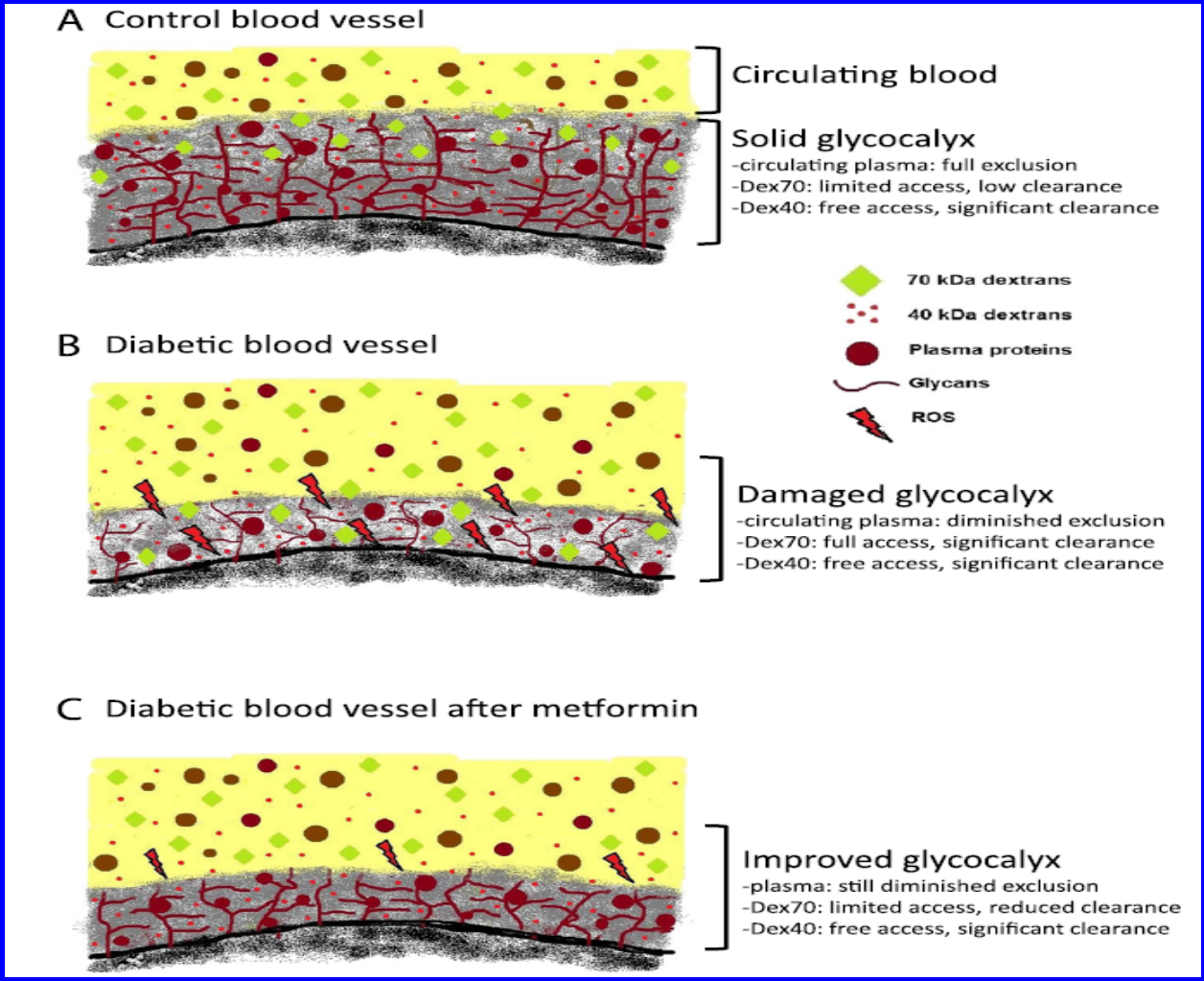
AstraZeneca receives Complete Response Letter from FDA May 27, 2016





JAMA 2014;312:2223-2233

Metformin Improves Whole-Body Glycocalyx Barrier Properties



Cardiovasc Diabetol 2013;12:175