Journal of Diabetes Science and Technology
Volume 3, Issue 4, July 2009

REVIEW ARTICLE

Antisense Oligonucleotide Therapy in Diabetic Retinopathy

Peter Hnik, M.D.,[1] David S. Boyer, M.D.,[2] Lisa R. Grillone, Ph.D.,[3] John G. Clement, Ph.D.,[1] Scott P. Henry, Ph.D.,[4] and Ellen A. Green, B.S.B./M.[1]

Abstract

Diabetic retinopathy is one of the leading causes of blindness in the United States and other parts of the world. Historically, laser photocoagulation and vitrectomy surgery have been used for the treatment of diabetic retinopathy, including diabetic macular edema. Both procedures have proven to be useful under certain conditions but have their limitations. New pathways and processes that promote diabetic retinopathy have been identified, and several new therapeutic approaches are under investigation. These new therapies may be beneficial in the treatment of diabetic retinopathy and include antivascular endothelial growth factor agents, corticosteroids, and therapies that may potentially target a number of additional diabetic retinopathy-related factors and processes, including antisense oligonucleotides. Second-generation antisense oligonucleotides, such as iCo-007, may offer a significant advantage in the treatment of diabetic retinopathy by downregulating the signal pathways of multiple growth factors that seem to play a critical role in the process of ocular angiogenesis and vascular leakage. Benefits of such molecules are expected to include the specificity of the kinase target and an extended half-life, resulting in less frequent intravitreal drug administration, resistance to molecule degradation, and a good safety profile.

J Diabetes Sci Technol 2009;3(4):924-930

Author Affiliations: [1]iCo Therapeutics Inc., Vancouver, British Columbia, Canada; [2]Retina-Vitreous Associates Medical Group, Beverly Hills, California; [3]PharmaQuest Associates, LLC, Carlsbad, California; and [4]Isis Pharmaceuticals, Carlsbad, California

Abbreviations: (AMD) age-related macular degeneration, (Ang-2) angiopoietin, (bFGF) basic fibroblast growth factor, (BRVO) branch retinal vein occlusion, (CMV) cytomegalovirus, (CRVO) central retinal vein occlusion, (DME) diabetic macular edema, (DR) diabetic retinopathy, (ETDRS) Early Treatment Diabetic Retinopathy Study, (EPO) erythropoietin, (HGF) hepatocyte growth factor, (ICAM) intercellular adhesion molecule, (MAP) mitogen-activated protein, (2′-MOE) 2′-*O*-methoxy-ethyl, (mRNA) messenger RNA, (siRNA) short interfering RNA, (TLR3) toll-like receptor 3, (VEGF) vascular endothelial growth factor

Keywords: antisense oligonucleotides, c-Raf kinase, diabetic macular edema, diabetic retinopathy, iCo-007, multiple proangiogenic factors, neovascular growth, vascular leakage

Corresponding Author: P. Hnik, M.D., M.H.Sc, iCo Therapeutics Inc., 760-777 Hornby Street, Vancouver, BC, V6Z 1S4 Canada; email address *hnik@icotherapeutics.com*