ACCORD Microvascular Outcomes

Though there are microvascular benefits that are associated with intensive glycemic therapy, clinicians should consider the increase in total and cardiovascular disease-related mortality, weight gain, and risk of severe hypoglycemia prior to implementing this strategy. Faramarz Ismail-Beigi, MD, PhD, Case Western Reserve University, Cleveland, OH, presented findings from a substudy of the Action to Control Cardiovascular Risk in Diabetes (ACCORD; NCT00000620) trial.

ACCORD included 10,251 participants with type 2 diabetes (T2DM), HbA1C concentrations >7.5%, and cardiovascular disease or >2 cardiovascular risk factors. Patients were randomized to receive either intensive (target HbA1C <6.0%; n=5128) or standard (target HbA1C 7.0% to 7.9%; n=5123) glycemic therapy. Intensive therapy was discontinued prior to study completion (after 3.7 years of the 5-year study) due to high mortality rates in that group. The intensive therapy group was then transitioned to standard treatment. The prespecified composite primary outcome was the development of renal failure (initiation of dialysis or end-stage renal disease, renal transplantation, or irreversible rise of serum creatinine >3.3 mg/dL) or diabetic eye complications (retinal photocoagulation or vitrectomy to treat diabetic retinopathy). This is similar to the microvascular outcomes in the UKPDS study [Holman RR et al. *New Engl J Med* 2008]. The second composite outcome consisted of the same components of the primary composite outcome with the addition of neuropathy (defined as Michigan Neuropathy Screening Instrument [MNSI] score ≥2.5). Thirteen additional nephropathy, diabetic eye complications, and neuropathy outcomes were also included in the final analysis. Outcome assessments were separated into two datasets—the period leading up to transition and the period from transition to study end.

Results were similar between the two glycemia treatment groups for the primary composite outcome of renal failure or diabetic eye complications throughout the duration of the study. The addition of neuropathy as part of the second composite outcome did not appear to impact the results, as there was no significant difference between the two groups for the first part of the trial (leading up to transition) or the second part of the trial (transition to study end).

There were interesting results pertaining to the 13 additional outcomes that merit consideration. Intensive therapy appeared to delay the onset of albuminuria as well as some measures of diabetic eye complications and neuropathy. The development of microalbuminura (urine albumin: creatinine ratio ≥30 mg/g) was more frequent in patients who were on standard therapy compared with those on intensive therapy (p=0.0005 until transition; p=0.0012 through the end of the study). Patients who received standard therapy also demonstrated higher rates of macroalbuminuria (urine albumin: creatinine ratio ≥300 mg/g) compared with those who received intensive therapy (p=0.0013 until transition; p=0.0003 through the end of the study). Using the Log MAR visual acuity chart, a 3-line decrease in visual acuity was observed more frequently in the standard therapy group over the course of the study (HR, 0.91; 95% CI, 0.83 to 1.00; p=0.0467).

In conclusion, intensive treatment of glycemia did not reduce the risk of composite measures of advanced microvascular outcomes. However, intensive therapy was associated with delayed onset of albuminuria and other measures of eye complications and neuropathy. Increased risk of total and cardiovascular-related mortality and severe hypoglycemia remains a concern and should be seriously evaluated when choosing an appropriate management strategy for patients with T2DM.

Additional Reading

Ismail-Beigi F et al. *Lancet* 2010.

Highlights from the

American Diabetes Association.

70th scientific sessions

JUNE 25-29, 2010 • ORLANDO, FL