a moderate-carbohydrate, low-fat diet based on former ADA recommendations. However, the reduction in HbA1C levels was marginally greater for all in the vegan group (p = .09) and significantly greater for those on a stable T2DM medication regimen (p = .01). Also, compared with 26% of the ADA group, 43% of the vegan group reduced the number of diabetes medications during the trial, mainly as necessitated by hypoglycemia [Barnard ND et al. *Diabetes Care* 2006].

The results of the Look AHEAD (Action for Health in Diabetes) study was also reviewed, which compared the effects of an intensive lifestyle intervention (ILI) with diabetes support and education (DSE) in T2DM [Look AHEAD Research Group. *Arch Intern Med* 2010]. Data showed that ILI resulted in a greater improvement in HbA1C than did DSE (–0.36% vs –0.09%; p< .001) over a 4-year period.

Consequently, the new recommendations note that the evidence is inconclusive regarding an ideal amount of carbohydrate intake for patients with diabetes, Dr. Yancy stated. He added that while the amount of carbohydrates and available insulin may be the most important factors that influence the glycemic response after eating, higher doses of insulin and several other diabetes medications can lead to unwanted effects, such as weight gain and hypoglycemia. Monitoring carbohydrate intake therefore remains key to glycemic control, and the new recommendations place emphasis on carbohydrate origin. Dr. Yancy concluded that for good health, carbohydrates should come from vegetables, fruits, whole grains, legumes, and dairy products, compared with other sources that contain added fats, sugar, or sodium.

Anti-VEGF Agents: Changing the Treatment Landscape for Diabetic Retinopathy

Written by Nicola Parry

In a symposium addressing current efforts to manage diabetic retinopathy, Lee M. Jampol, MD, Northwestern University, Chicago, Illinois, USA, provided an update on some key trials conducted by the Diabetic Retinopathy Clinical Research Network (DRCR.net), including important contributions from Protocol I. This study showed that anti-vascular endothelial growth factor (VEGF) therapy as an initial strategy should be the gold standard of treatment for diabetic macular edema (DME).

For decades, focal laser photocoagulation was the standard of care, and was highly effective, for treatment of DME. However, this technique is time-consuming and is sometimes associated with loss of central vision. In recent times, anti-VEGF agents have revolutionized the management of these conditions by targeting VEGF, an angiogenic mitogen with a pivotal role in the pathogenesis of DME.

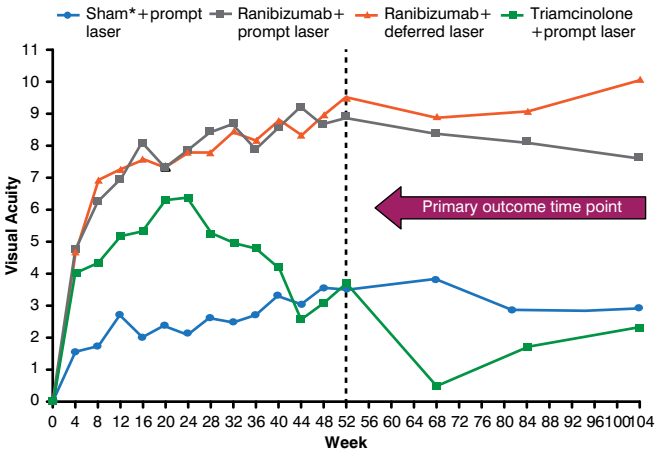
One of the most important studies from DRCR.net is Protocol I, a randomized, controlled trial, which evaluated the efficacy of

- intravitreal ranibizumab 0.5 mg in combination with prompt or deferred (after 6 months) laser photocoagulation,
- prompt focal/grid laser treatment alone for treatment of central involvement DME, and
- intravitreal triamcinolone acetonide 4 mg with prompt laser treatment.

In total, 691 patients (854 eyes) with central-involvement DME were enrolled.

After 1 year, eyes treated with intravitreal ranibizumab and prompt or deferred laser had better visual acuity (VA) letter scores compared with focal laser with sham injection. The mean change in VA from baseline was significantly greater in the ranibizumab plus prompt laser group (p< .001) and ranibizumab plus deferred laser group (p< .001), but not in the triamcinolone plus prompt laser group (p = .31; Figure 1).

Figure 1. Mean Change in Visual Acuity



p values for difference in mean change in visual acuity from sham+prompt laser at the 52-week visit: ranibizumab+prompt laser <.001; ranibizumab+deferred laser <.001; and triamcinolone+prompt laser =.31.

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*On November 21, 2014, this was changed from Sharm to Sham.

Visual acuity benefit often cannot be maintained in neovascular age-related macular degeneration if the frequency of ranibizumab injection is decreased from a monthly injection protocol. However, Protocol I demonstrated benefit with the use of anti-VEGF therapy for DME. Data showed that improved VA was maintained in these patients for more than 3 years of follow-up despite a decreasing number of intravitreal injections of ranibizumab: a median of 6 injections for the first 6 months, 3 injections in the second 6 months, 2 to 3 injections in the second year, and 1 to 2 injections in the third year [Diabetic Retinopathy Clinical Research Network *Ophthalmology* 2012; 2010].

Additional DRCR.net research in this field is underway. Protocol S and Protocol T are near completion. The noninferiority Protocol S study is comparing 2-year VA outcomes in patients with proliferative diabetic retinopathy treated with anti-VEGF therapy plus deferred panretinal photocoagulation (PRP) or standard, prompt PRP therapy. Protocol T is a comparative effectiveness study of three intravitreal anti-VEGF agents—aflibercept, bevacizumab, and ranibizumab—in patients with DME. The primary outcome is mean change in VA.

Treatment of Gestational Diabetes Improves Short-Term Outcomes in Offspring

Written by Nicola Parry

Matthew W. Gillman, MD, Harvard Medical School, Boston, Massachusetts, USA, discussed the relation between gestational diabetes mellitus (GDM) and macrosomia, neonatal morbidity, and childhood obesity. He shared data demonstrating that treatment of GDM improves short-term fetal and neonatal outcomes, but does not reduce obesity in offspring at the age of 4 to 5 years.

As the global pandemic of diabetes continues, increasing numbers of women of childbearing age are at risk for GDM and type 2 diabetes mellitus (T2DM). GDM may contribute to an intergenerational cycle of obesity and diabetes: A woman who enters pregnancy overweight or obese may gain excessive weight and retain more postpartum, leading to T2DM and cardiovascular disease (CVD) in the long term. Fetal growth and metabolism may also be altered, leading to child obesity.

Dr. Gillman discussed two trials that addressed the value of glucose control in GDM, both of which randomized ~1000 patients to therapy or observation. In the Australian Carbohydrate Intolerance Study in Pregnant Women [ACHOIS], the composite end point of serious perinatal outcomes included fetal death, bone fracture, shoulder dystocia, and nerve palsy [Crowther CA et al. *N Engl J Med* 2005]. In the study conducted within the Maternal–Fetal Medicine Units (MFMU) Network, the composite end point was stillbirth or perinatal death and neonatal complications, including hyperbilirubinemia, neonatal hypoglycemia, and hyperinsulinemia [Landon MB et al. *N Engl J Med* 2005].

In the ACHOIS study, there was a decrease in the main outcome measure of any serious perinatal complication with intervention (RR, 0.33; 95% CI, 0.14 to 0.75; $p = .01$). However, the MFMU study composite outcome was not significantly changed ($p = .14$). The incidence of large-for-gestational age (LGA) decreased significantly in both studies ($p < .001$), whereas shoulder dystocia was only significantly decreased in the MFMU study ($p = .02$). In both trials, maternal weight gain from diagnosis to term was significantly lower with intervention (mean 1.7 kg less in ACHOIS, $p = .01$; 2.2 kg less in the MFMU study, $p < .001$), yet birth injury and small-for-gestational age were not significantly changed.

The results of both trials indicated the benefits of treating mild to moderate GDM, in particular with respect to reduced incidences of macrosomia and LGA. Subsequent meta-analyses and reviews have also provided broad agreement on these benefits and risks, noted Dr. Gillman.

Since GDM has been hypothesized to cause obesity in offspring, a longer-term follow-up study of a subset of children from the ACHOIS trial compared the effect of treatment for mild GDM with routine care on the body mass index (BMI) of children aged 4 to 5 years. The main outcome was age- and sex-specific BMI. Although treatment of GDM substantially reduced macrosomia (5.3% vs 21.9%), there was no reduction in their mean BMI at age 4 to 5 years (0.49 in treatment vs 0.41 in routine care) [Gillman MW et al. *Diabetes Care* 2010].

Studies so far have therefore shown that GDM treatment reduces serious fetal and neonatal outcomes in the short term but do not show similar benefits in the longer term. However, the long-term findings are based on only 1 study. Additionally, GDM may affect weight in early infancy and again in later childhood, but not in early childhood; thus, even longer-term follow-up studies are required to address this question, Dr. Gillman concluded.