Results from the ACCORD BP Trial

Intensive blood pressure (BP) control did not reduce the rate of a composite outcome of major cardiovascular (CV) events in high-risk patients with type 2 diabetes mellitus (DM), according to the Action to Control Cardiovascular Risk in Diabetes (ACCORD; NCT00000620) Blood Pressure Trial. William C. Cushman, MD, VA Medical Center, Memphis, TN, presented the results of the ACCORD BP Trial.

The ACCORD BP Trial included 4733 patients with stable type 2 DM > 3 months (average duration 10 years), with hemoglobin A1c 7.5% to 11%, who were considered to be at high risk for CVD (defined as clinical or subclinical disease or ≥ 2 CV risk factors, in addition to DM). Patients were randomized to receive either intensive therapy (n=2362) (initial 2-drug therapy of thiazide-type diuretic plus an angiotensin-converting enzyme inhibitor (ACEI), an angiotensin receptor blocker (ARB), or a β-blocker was recommended with drugs added or titrated at each visit in order to achieve a systolic BP (SBP) of <120 mmHg) or standard therapy (n=2371) (where therapy was intensified if SBP was ≥160 mmHg at one visit or ≥140 mmHg during two consecutive visits; therapy was down-titrated if SBP was <130 mmHg at one visit or <135 mmHg during two consecutive visits). The target SBP for the intensive therapy group was <120 mmHg, and the target SBP in the standard therapy group was <140 mmHg.

The primary outcome was the first occurrence of a major CV event (defined as nonfatal myocardial infarction [MI], nonfatal stroke, or CV death). Secondary outcomes included an expanded macrovascular outcome (defined as a combination of the primary outcome plus revascularization or hospitalization for congestive heart failure), major coronary disease events (defined as a combination of a fatal coronary event, a nonfatal MI, or unstable angina), hospitalization or death due to heart failure, all stroke, death from any cause, or death from CV causes.

The rate of serious adverse events, although infrequent, was significantly higher in those who were treated with intensive therapy compared with those who received standard therapy (3.3% vs 1.3%, respectively; p<0.001). Additionally, the mean estimated glomerular filtration rates were significantly lower in the intensive therapy group (75 vs 81mL/min/1.73m^2; p<0.001), but the incidence of end-stage renal disease was no different. One year from study end, the mean SBP averaged 119.3 mmHg versus 133.5 mm Hg for intensive and standard groups, respectively, which amounted to a difference of 14.2 mmHg.

The annual rate of the composite of fatal and nonfatal CV events was similar in both groups (1.87% vs 2.09% per year for standard therapy; p=0.20). There was no difference in death from any cause between the two groups. Interestingly, the prespecified secondary outcomes of total stroke (p=0.01) and nonfatal stroke (p=0.03) were lower in the intensive therapy group. No interaction within predefined subgroups was found, although there was a trend (p<0.08) for modification of effect by randomization to intensive or standard glycemia intervention, with benefit in the standard group.

These results failed to demonstrate that lower target SBP (<120 mmHg), through the use of intensive therapy, reduces the rate of fatal and nonfatal CV events (composite primary endpoint) in high-risk patients with type 2 DM.

Further Reading: The ACCORD Study Group *N Engl J Med* 2010; published online ahead of print.

Results from the NAVIGATOR Trial

There is no evidence of cardiovascular (CV) benefit that is associated with long-term treatment with nateglinide and valsartan in patients with impaired glucose tolerance and cardiovascular disease (CVD) or CV risk factors. However, valsartan therapy is associated with a reduction in the incidence of diabetes. Rury R. Holman, MB, ChB, FRCP, Churchill Hospital, Oxford, United Kingdom, and Robert M. Califf, MD, Duke Translational Medicine Institute, Durham, NC, presented results from the Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR; NCT00097786) Trial.

NAVIGATOR was a double-blind, randomized, multicenter, controlled trial that included 9306 patients with impaired glucose tolerance, defined as fasting plasma glucose (FPG) ≥95 mg/dL and <125 mg/dL and either known CVD if ≥50 years old or ≥1 risk factor for CVD if ≥55 years old. The use of any antidiabetic agent within the last 5 years was an exclusion. Patients were randomized in a 2x2 factorial design to either valsartan (an angiotensin receptor blocker) 160 mg daily or placebo, and to either nateglinide (a short-acting secretagogue) 60 mg 3 times daily or placebo. All study subjects participated in a lifestyle modification program throughout the duration of the study.

One-quarter of participants had known CVD at baseline. The mean age was 64 years, and the median follow-up was 6.5 years for vital status and 5.0 years for incident diabetes. On average, patients in this study were obese at baseline (average BMI 30.5 kg/m^2). The three coprimary endpoints for both comparisons of this study were:

1. The incidence of diabetes, defined as fasting plasma glucose (FPG) ≥126 mg/dL (≥7.0 mmol/L) and/or 2-hour plasma glucose ≥200 mg/dL (≥11.1 mmol/L), confirmed by oral glucose tolerance test within 12 weeks;