

An Endocrine Society Statement to Providers on Study Findings Related to Treatment of Hypertension in Patients with Diabetes

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On March 14, three studies presented at an American College of Cardiology meeting raised questions about whether normalization of blood pressure in hypertensive patients with diabetes or those with impaired glucose tolerance and cardiovascular risk factors could lead to a reduction in the rate of cardiovascular events. Two of these papers, covering findings from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) blood pressure trial (ACCORD BP) and Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) trial, were simultaneously published on-line in the *New England Journal of Medicine*.

These studies do not advise against the treatment of hypertension in patients with diabetes; the controversy concerns the target level to which blood pressure should be reduced in these patients. The conclusions of the ACCORD BP study suggest that achieving a systolic blood pressure of 120 mm Hg compared to 140 mm Hg does not reduce the rate of major cardiovascular events. Furthermore, systolic blood pressure levels in the intensive treatment arm of the study were associated with more adverse events, including higher rates of hypokalemia and elevations of serum creatinine. The NAVIGATOR study similarly concludes that the addition of Valsartan to the treatment regimen for patients with impaired glucose tolerance did not reduce the rate of cardiovascular events. The final study, INVEST, evaluated a control group compared to a moderate blood pressure group and an intensive blood pressure group in hypertensive diabetic patients with heart disease. While the greatest morbidity and mortality was seen in the control group, there was an increase in mortality in the intensively treated group compared to the moderate blood pressure control group, though this finding was restricted to those who achieved systolic blood pressure less than 115 mm Hg.

In interpreting these findings, The Endocrine Society recommends that practitioners consider several points. First, the INVEST study has only been presented in abstract form and has not yet been through the formal peer review process leading to publication. Second, the ACCORD BP and NAVIGATOR studies evaluated patients with modest degrees of hyperglycemia and hypertension, so extrapolating the results from the latter two papers to patients with more significant hyperglycemia and hypertension could be problematic. Moreover, in the NAVIGATOR trial, the achieved difference in blood pressure between the group that received Valsartan and the control group was only 2.8/1.4 mm Hg, a difference that may be too small to lead to differences in cardiovascular outcomes.

It should also be noted that the ACCORD BP study found some significant improvements in secondary outcome measures. Total strokes were reduced by 41% in the intensively managed group compared to controls (from 0.53% to 0.32%).

The Endocrine Society continues to support the treatment of hypertension in patients with diabetes and recommends that patients should not modify or discontinue antihypertensive medications without consulting their physicians. While a systolic blood pressure target below 140 mm Hg in hypertensive patients with diabetes remains a reasonable goal and seems consistent with the findings of these new studies, reductions in blood pressure below this level might not afford much additional cardiovascular benefit. Furthermore, aggressive systolic blood pressure targets below 120 mm Hg may be detrimental. In light of these studies, the current Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) and American Diabetes Association recommendations (less than 130/80 mm Hg for patients with

diabetes) seem prudent for many, but not all patients. In patients with significantly higher blood pressure and blood sugar than the subjects in these studies, the optimum blood pressure goal remains to be defined.

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