

## ADVANCE reveals new insights in the fight against severe diabetes complications

**Montreal, Canada, 20 October 2009** – New results from ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicon MR Controlled Evaluation), the largest clinical trial ever performed in patients with type 2 diabetes worldwide, provide important insights into the therapeutic strategy to adopt for efficient and safe blood glucose control aimed at the reduction of severe diabetes complications.<sup>1</sup>

The new data from ADVANCE, presented today at the International Diabetes Federation (IDF) Congress, show that the efficacy and safety of intensive blood glucose control using gliclazide modified release (MR) (Diamicon MR)-based regimen is maintained across a broad range of patients in different clinical settings.<sup>1</sup>

ADVANCE demonstrated that intensive glucose control with a gliclazide MR-based treatment regimen in people with type 2 diabetes reduces the combined risk of microvascular and macrovascular events, primarily through reductions in the risk of diabetic nephropathy.<sup>2</sup>

*"Intensive glucose control with a gliclazide MR-based regimen was effective in lowering HbA<sub>1C</sub>, irrespective of age, duration of diabetes, sex, body mass index, or HbA<sub>1C</sub> at study entry, and also irrespective of initial glucose lowering treatment,"* said ADVANCE Study Investigator Sophia Zoungas from The George Institute for International Health, Australia. *"The gliclazide MR-based regimen was well-tolerated with very low rates of severe hypoglycemia and no weight gain."*

ADVANCE showed a positive trend toward a reduction of major cardiovascular events in diabetes patients who received intensive glucose control.<sup>2</sup> This finding was supported in a recent collaborative meta-analysis of 4 trials of intensive glucose lowering, including ADVANCE and ACCORD, which demonstrated a significant 9% reduction in major cardiovascular events, primarily reflecting a 15% reduction in myocardial infarction.<sup>3</sup> On the basis of observational data, several national registers (including more than 70,000 patients with type 2 diabetes), have recently reported that glucose lowering regimens that included gliclazide were associated with lower risks of mortality compared to other therapeutic strategies.<sup>4,5</sup>

*"ADVANCE is a huge reservoir of valuable clinical information,"* concluded ADVANCE Principal Investigator Professor John Chalmers from The George Institute for International Health, Australia. *"For this reason, we plan to continue the follow-up of the ADVANCE patients and we believe that this new study—ADVANCE-ON<sup>6</sup>— will play a pivotal role in defining future clinical management of the tens of millions of people with type 2 diabetes worldwide."*

### Additional new data

At the IDF Congress, the ADVANCE investigators also provided important insights into factors predicting cardiovascular risk in this population.<sup>7</sup>

Age at diagnosis, known duration of diabetes, sex, pulse pressure, treated hypertension, atrial fibrillation, retinopathy, HbA<sub>1C</sub>, albumin/creatinine ratio, and non-HDL cholesterol level at baseline were all found to be significant predictors of cardiovascular events. A new risk prediction tool was developed by the ADVANCE investigators using these variables, paving the way for a new

'risk engine' that may be more relevant for contemporary populations of treated patients with diabetes compared to older risk prediction tools such as the Framingham and UKPDS (United Kingdom Prospective Diabetes Study) models.<sup>7</sup>

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### **Notes to editor:**

ADVANCE was designed, conducted, monitored, analyzed, and reported by a collaborative medical research group supported by the Australian Government's National Health and Medical Research Council after full peer review. The study was carried out independently of the industry sponsor, and the Management Committee—whose membership did not include any industry representatives—had final responsibility for the reporting of results.

The first part of ADVANCE investigated the effects of intensive blood pressure lowering on outcome using a fixed combination of perindopril and indapamide. The results were published in 2007. Reference: ADVANCE Collaborative Group; Patel A, MacMahon S, Chalmers J, Neal B, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet*. 2007;370:829-840.

The second part of ADVANCE investigated the effects of intensive glucose control with a gliclazide MR-based regimen and the main results were published in 2008. These demonstrated that intensive control reduced the combined major macrovascular and microvascular end point (18.1% vs. 20.0%; hazard ratio (HR) 0.90; 95% confidence interval 0.82 to 0.98;  $P=0.013$ ). Major microvascular events were reduced (9.4% vs. 10.9%; HR 0.86 [0.77 to 0.97];  $P=0.014$ ), primarily because of a reduction in nephropathy (4.1% vs. 5.2%; HR 0.79 [0.66 to 0.93],  $P=0.006$ ), with no significant effect on retinopathy ( $P>0.1$ ). Reference: ADVANCE Collaborative Group; Patel A, MacMahon S, Chalmers J et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *NEJM* 2008; 358: 2560-2572

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**The National Health & Medical Research Council of Australia** is the Australian Government's peak body for supporting health and medical research; for developing health advice for the Australian community, health professionals, and governments; and for providing advice on ethical behavior in health care and in the conduct of health and medical research.

The research funding arm of French pharmaceutical company Servier is the **Institut de Recherche International Servier**.

### **References**

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