

## LARGEST EVER TRIAL CONDUCTED IN PATIENTS WITH TYPE 2 DIABETES COMPLETE

*“ADVANCE will have huge implications for care of patients worldwide”*

19 May 2008 – ADVANCE (Action in Diabetes and Vascular Disease), the largest clinical trial ever performed in patients with type 2 diabetes worldwide, is now complete. The second and final part of this five-year trial investigates the effect of intensive blood glucose lowering treatment on major macrovascular (cardiovascular death, MI, stroke) and microvascular (kidney and eye disease) events.

Over 11,000 patients were randomised and more than 20 countries participated in ADVANCE. The final patient visits were made at the end of January 2008, the database is now closed and main analysis complete. The data from the blood glucose lowering arm of ADVANCE will be presented for the first time at the American Diabetes Association Scientific Sessions on 6 June 2008 in San Francisco, USA.

Globally, there are approximately 250 million people with diabetes, most of who will eventually be killed or disabled by the complications of their condition. It is estimated that by 2025 the number of individuals with diabetes will rise to 380 million. The most common cause of death in people with diabetes is heart disease. Kidney disease also affects a large proportion. In 2006, the United Nations issued a statement calling for increased international action to combat the global epidemic of diabetes.

“People with diabetes have a two to four-fold greater risk of experiencing a cardiovascular event compared to non-diabetics. However, despite this high risk, there is surprisingly little evidence about the role of intensive blood glucose control in the prevention of diabetic vascular disease”, points out the ADVANCE Principal Investigator Professor John Chalmers from The George Institute for International Health, Sydney.

“ADVANCE will provide new and robust evidence on whether intensive glucose lowering treatment improves outcomes and could have huge implications for the practical management of type 2

diabetes worldwide”, says ADVANCE Study Director Associate Professor Anushka Patel also from The George Institute.

ADVANCE was designed to answer two questions: first, does intensive treatment to lower blood pressure improve outcome; and second, does intensive treatment to reduce blood glucose improve outcome. The first question was answered by the results of the blood pressure lowering arm of the study in which a treatment regimen including the fixed combination of the ACE inhibitor perindopril and the diuretic indapamide was shown to reduce mortality in patients with diabetes. The results of glucose-lowering arm, (based on gliclazide modified release, MR and a range of other drugs) of the ADVANCE study will provide the answer to the second question when announced later this year.

ADVANCE was conducted in 215 clinical centres selected from Australasia, Asia, Europe and North America. The trial randomised 11,140 high risk type 2 diabetes patients and the primary end-point was a composite of major macro vascular (cardiovascular death, MI, stroke), and micro vascular complications (kidney and eye disease).

In the intensive glucose lowering arm of the study, patients received 1 – 4 tablets of gliclazide MR (30 – 120 mg) daily together with other glucose control medications. The aim of this regimen was to achieve a haemoglobin A1c (HbA1c), a measure of glucose control, of  $\leq 6.5\%$ . Treatment was continued until the completion of follow-up (five years).

Due to the early release of results by another similar large trial of diabetes patients, in February the ADVANCE Data Safety Management Board announced that interim results from ADVANCE provided no evidence of safety issues among patients receiving the intensive glucose control regimen. The study was accordingly closed out according to the planned schedule. The full results of ADVANCE will define the overall balance of benefits and risks of intensive glucose lowering treatment.

The ADVANCE study was designed and conducted by an independent collaborative group of medical researchers co-sponsored by The George Institute for International Health at the University of Sydney, the National Health & Medical Research Council of Australia and Servier International.

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For further information, please contact:

Emma Orpilla – Public Relations, The George Institute for International Health

Tel: +612 9993 4500/ Mobile: +61410 411 983

Fax: +612 9993 4501/ email: [eorpilla@george.org.au](mailto:eorpilla@george.org.au)

[www.thegeorgeinstitute.org.au](http://www.thegeorgeinstitute.org.au)

Sarah Ballard / Moira Gitsham

Tonic Life Communications

Tel: +44 207 798 9900

E-mail: [sarah.ballard@toniclc.com](mailto:sarah.ballard@toniclc.com) / [moira.gitsham@toniclc.com](mailto:moira.gitsham@toniclc.com)

[www.advance-trial.com](http://www.advance-trial.com)

### Notes to editor:

The George Institute for International Health is an internationally-recognised health research organisation, undertaking high impact research across a broad health landscape. It is a leader in the clinical trials, health policy and capacity-building areas.

ADVANCE is an independent investigator-initiated study and was funded by grants from the National Health and Medical Research Council of Australia and Servier

The research funding arm of French pharmaceutical company Servier is the Institut de Recherche International Servier. Diamicon MR is the international brand name for gliclazide modified release, registered by Servier in some countries also as Diamicon 30 mg, Diagluclide MR 30mg, Gluctam MR 30 mg, Diaprel MR, Diabeton MR, Diamicon Uno 30 mg, Diabeton MB, Uni Diamicon, Diamicon LM 30 mg, Unidiamicon, Dianormax MR, Diamicon MR Tablets 30 mg, Diamicon 30 mg MR, Dramion 30mg.

### Reference:

1. 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;370:829-40.