



THE LARGEST EVER STUDY OF DIABETES SHOWS INTENSIVE GLUCOSE CONTROL REDUCES SERIOUS COMPLICATIONS

“ADVANCE results go beyond existing evidence”

San Francisco, USA, 6 June 2008 – New results from the world’s largest ever study of diabetes treatments show that intensive blood glucose (sugar) control using modified release gliclazide and other drugs as required, protects patients against serious complications of the disease. In particular, intensive treatment reduces the risk of kidney disease by one-fifth. Presented today at the American Diabetes Association and published in the *New England Journal of Medicine*, the results of ADVANCE (Action in Diabetes and Vascular Disease) show that this intensive treatment strategy has the potential to benefit millions of diabetic patients worldwide.

Diabetes mellitus is one of the greatest threats to the health of populations worldwide. Globally, there are approximately 250 million people with diabetes and that number is estimated to rise to 380 million in 2025.

Chief investigator of the study, Professor Stephen MacMahon, Principal Director of The George Institute, Australia said “We are facing a global epidemic of diabetes. The ADVANCE results go beyond existing evidence as we have now shown that reducing the haemoglobin A1c level (a marker of blood glucose control) to 6.5% is a safe and effective way to reduce serious complications, particularly the risk of kidney disease, one of the most serious and disabling consequences of diabetes, leading to death in one in five people with diabetes.”

“Hypoglycemia (low blood sugar) was uncommon in the ADVANCE study, although as expected it was more frequent among those receiving intensive treatment,” pointed out Study Director, Associate Professor Anushka Patel from The George Institute. “These findings reinforce that blood glucose lowering in diabetes is safe and has an important role to play in the prevention of serious complications.”

“Moreover, in contrast to the recently halted ACCORD study, there was no evidence whatsoever of any increased risk of death among those receiving intensive treatment in ADVANCE.”

ADVANCE was initiated and designed by physicians at Australia's George Institute for International Health and involved a group of independent medical researchers from 20 countries worldwide. The study involved 11,140 patients with type 2 diabetes who were treated and followed up for five years. The study aimed to reduce levels of haemoglobin A1c to 6.5% or below. Intensive treatment included the sulfonylurea, modified-release gliclazide, for all patients and other drugs as required to achieve the haemoglobin target.

The major findings of ADVANCE show that intensive blood glucose lowering treatment:

- Safely controlled blood glucose to a mean HbA1c level of 6.5%
- Significantly reduced the overall risk of serious diabetes complications (by 10%), with a one-fifth reduction in kidney disease (21%) and 30% reduction in the development of proteinuria, a well established marker of increased cardiovascular risk.
- Achieved a positive trend towards reduction in the risk of cardiovascular death (12%), although not statistically significant.

"Today, it is clear that the prevention of major vascular complications of diabetes requires a multi-factorial approach addressing all modifiable risk factors" concluded Professor John Chalmers, chairman of the study management group, "among which an intensive glucose control plays an important role, in particular in protecting the kidneys".

ENDS

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

www.thegeorgeinstitute.org.au

Sarah Ballard / Moira Gitsham

Tonic Life Communications

Tel: +44 207 798 9900

E-mail: sarah.ballard@toniclc.com / moira.gitsham@toniclc.com

www.advance-trial.com

Notes to editor:

ADVANCE was designed, conducted, monitored, analysed 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.

Confidence Intervals: Intensive control reduced the combined major macrovascular and microvascular endpoint (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 ($p>0.1$).

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 last year. 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; 370:829-40.

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. The Institute has a global network of top medical experts in a range of research fields as well as expertise in research design, project management and data and statistical analysis. With a respected voice among global policy makers, The Institute has attracted significant funding support from governments, philanthropic organisations and corporations. George Institute research is regularly published in the top tier of academic journals internationally.

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 behaviour 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**.

Management committee and investigators of the ADVANCE trial:

- John Chalmers, Senior Director, The George Institute for International Health Emeritus Professor of Medicine, The University of Sydney Emeritus Professor of Medicine, Flinders University Australia;
- Stephen MacMahon, Principal Director, The George Institute for International Health Professor, Cardiovascular Medicine and Epidemiology, The University of Sydney Australia;
- Anushka Patel Director, Cardiovascular Division, The George Institute for International Health, MD, Cardiovascular Medicine, Royal Prince Alfred Hospital, Sydney Australia
- Diederick E. Grobbee, Professor, Clinical Epidemiology, Utrecht University Director, Julius Center for Health Sciences and Primary Care Netherlands
- Pavel Hammet, Director, Laboratory of Molecular Medicine, Centre hospitalier de l'Université de Montréal Professor, Department of Medicine at the Université de Montréal Canada
- Stephen Harrap, Head, Department of Physiology Professor, Department of Physiology, University of Melbourne Australia
- Li-Sheng LIU, President, World Hypertension League; President, Chinese Hypertension League, Director, Clinical Trials and Research Centre, Chinese Hypertension League, Beijing, China
- Neil R Poulter, Professor of Preventive Cardiovascular Medicine Imperial College London United Kingdom
- Mark E Cooper, Director, Danielle Alberti Centre for Diabetes Complications Head, Vascular Division - Baker Heart Research Institute Australia
- Eleuterio Ferrannini, Professor, Department of Internal Medicine, University of Pisa Italy
- Paul Glasziou, Director, Centre for Evidence-Based Medicine, Department of Primary Health Care, University of Oxford, United Kingdom

- Simon Heller, Professor, Clinical Diabetes, University of Sheffield
Director, Research and Development, Sheffield Teaching Hospitals Foundation Trust
United Kingdom
- Guiseppe Mancia, Head, Division and Department of Internal Medicine, San Gerardo Hospital,
Monza, Chairman, Department of the Clinical Medicine and Prevention, University of Milan-
Bicocca, Italy
- Michel Marre, Head, Endocrinology, Diabetology and Metabolic Disorders Department, Bichat-
Claude Bernard Hospital, France
- Carl Erik Mogensen, Professor of Medicine, Medical Department M (Diabetes &
Endocrinology), Aarhus University Hospital, Denmark
- Bruce Neal, Senior Director, Research and Development, The George Institute for International
Health, Associate Professor, Faculty of Medicine, University of Sydney, Australia
- Chang Yu PAN, Professor, Department of Endocrinology, Beijing 301 Hospital
China
- Anthony Rogers, Director, Clinical Trials Research Unit, Professor of Epidemiology, Director,
Clinical Trials Research Unit, School of Population Health, The University of Auckland, New
Zealand
- Bryan Williams, Professor of Medicine, School of Medicine, University of Leicester
Consultant Physician, University Hospitals Leicester, Leicester Hypertension Clinic
United Kingdom
- Mark Woodward, Professor of Medicine and Director, Biostatistics Core, Department of
Medicine, The Mount Sinai Medical Center, New York, USA