

## Letter

David Dunger, MD; University of Cambridge, Cambridge, UK

M. Loredana Marcovecchio, MD; University of Cambridge, Cambridge, UK

John Deanfield, MD; UCL Institute of Cardiovascular Science

*Jonnalagadda et al* asked some clarifications on how the AddIT results are reported.

Data are displayed in table 1 and in all figures following the 2X2 factorial design, thereby the 'ACE inhibitor arm' combines participants from the 'ACE inhibitor plus placebo' and 'ACE inhibitor plus statin' groups, whereas the matched 'placebo arm' combines the 'placebo plus placebo' and 'statin plus placebo' groups. The same format was used for the statin analysis. The exception is table 2 reporting the adverse events for the four individual groups in order to show those more likely associated with one of the two trial drugs.

The potential interaction between ACE inhibitor and statin was assessed and was not statistically significant.

*In reply to Mei:* the AddIT trial was designed to assess the short-term effects of ACE inhibitors and statins on renal, retinal and cardiovascular outcomes in adolescents with type 1 diabetes. However, we agree that these early interventions could have beneficial effects later in life through a 'legacy effect', as previously reported in glucose- or blood-lowering drug trials<sup>1,2</sup>.

Funding for follow up of AddIT trial participants along with the parallel observational cohort is currently being sought. We plan to follow participants up to 5 years from the end of the trial, when the study population will be entering the second/third decade of diabetes and the first direct evidence of vascular complications are observed<sup>3</sup>. That will allow us to detect potential long-term effects on albuminuria/decline in renal function, retinopathy as well as cardiovascular outcomes.

*In response to Flynn:* we agree that ambulatory blood pressure monitoring (ABPM) provides a better and more complete assessment of blood pressure and its circadian rhythm. Indeed, earlier studies have shown that loss of the nocturnal blood pressure dip<sup>4</sup>, or early increases

in ambulatory blood pressure<sup>5</sup>, are associated with urinary albumin excretion in young people with type 1 diabetes.

However, the selection of study participants for the AdDIT trial was primarily based on increased urinary albumin excretion and not on their blood pressure status, although potential participants with established hypertension unrelated to diabetic nephropathy were excluded. Therefore, ABPM at baseline was not required for patient selection or stratification in terms of effects on the primary outcome.

Blood pressure was one of the trial secondary outcomes, and we agree that ABPM could have allowed us to detect more subtle changes in blood pressure or effects of treatments on this cardiovascular marker.

#### Reference

1. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 2008;359(15):1577–89.
2. Zoungas S, Chalmers J, Neal B, et al. Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes. *N Engl J Med* 2014;371(15):1392–406.
3. James S, Gallagher R, Dunbabin J, Perry L. Prevalence of vascular complications and factors predictive of their development in young adults with type 1 diabetes: systematic literature review. *BMC Res Notes* 2014;7:593.
4. Lurbe E, Redon J, Kesani A, et al. Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. *N Engl J Med* 2002;347(11):797–805.
5. Marcovecchio ML, Dalton RN, Schwarze CP, et al. Ambulatory blood pressure measurements are related to albumin excretion and are predictive for risk of microalbuminuria in young people with type 1 diabetes. *Diabetologia* 2009;52(6):1173–81.