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9th February 2010

Dr Martyn Ward
Head of Clinical Trials Unit
MHRA
Market Towers
1 Nine Elms Lane
London
SW8 5NQ

Dear Dr Ward,

Re: Doppler ultrasound investigation of microvasculature in health and disease
MHRA Reference: 21374/0203/001-0001
Ethics Reference: 06087GM-A
EudraCT number: 2006-005406-32

End of trial study report

This trial commenced on 15th August 2007 and was completed on 1st December 2009. The trial was completed satisfactorily with no incidents of note.

Recruitment

104 subjects were recruited in total. This comprised 39 subjects with type 1 diabetes mellitus, 25 subjects with hypertension and 40 healthy controls.

Numbers receiving investigational medicinal product

Of the subjects with diabetes, 3 were not given medication due to hypotension at baseline, 1 was unwilling to take medication and 1 was excluded due to an abnormality detected during ultrasound examination. Thus, 34 subjects with diabetes were issued with an investigational medicinal product. 16 received ramipril and 18 received bendroflumethiazide. 13 of those receiving ramipril completed the study; 2 were lost to follow-up; and 1 withdrew from the study due to a non-serious adverse drug reaction. 16 of those receiving bendroflumethiazide completed the study; 1 was lost to follow-up; and 1 withdrew from the study due to a non-serious adverse drug reaction.

Of the subjects with hypertension, 5 were unwilling to take medication. Thus, 20 subjects with hypertension were issued with an investigational medicinal product. 9 received ramipril and 11 received bendroflumethiazide. All of those receiving ramipril completed

the study. 9 of those receiving bendroflumethiazide completed the study; 2 were lost to follow-up.

Adverse events

3 adverse events were recorded during the trial. All were minor. 1 subject taking bendroflumethiazide developed minor leg cramps. 1 subject taking ramipril developed a dry cough. 1 subject attended the local emergency department with palpitations – this was deemed non-serious and she was not admitted to hospital.

Trial outcomes

Useful data on blood vessel function was captured from healthy controls and compared with that from subjects with diabetes and hypertension. The effect of drug intervention on subjects with disease was captured. The results have subsequently been presented successfully in a thesis for the degree of Doctor of Medicine. Papers are currently being written for submission to peer reviewed journals.

If any other information is required, I would be happy to provide this.

Yours faithfully,

Professor Gary McVeigh

Cc:

Dr Theresa Donaldson, Chair, HPSS REC 2

Ms Alison Murphy, Belfast City Hospital Research Office