Date 24/04/12 Final Report to MHRA

EudraCT No.: 2007-004529-57

REC No.: 07/NIR03/92

Vascular Pleiotrophic Effects of Bisphosphonates in Postmenopausal Women: Cellular Mechanisms and Functional Consequences.

This study was a randomised double blind placebo controlled trial involving the use of Risedronate in post-menopausal women with osteoporosis. Women with a diagnosis of osteoporosis received either Risedronate or placebo for 24 weeks. Vascular measures of endothelial function were examined before and after treatment. It used a licensed medicinal product according to its appropriate indications

Sponsor: Belfast Health and Social Care Trust and Queens University Belfast

Protocol version 1.4

Start date: 1st August 2007

End date: February 2011

Chief Investigator: Professor Gary McVeigh

Study Objectives

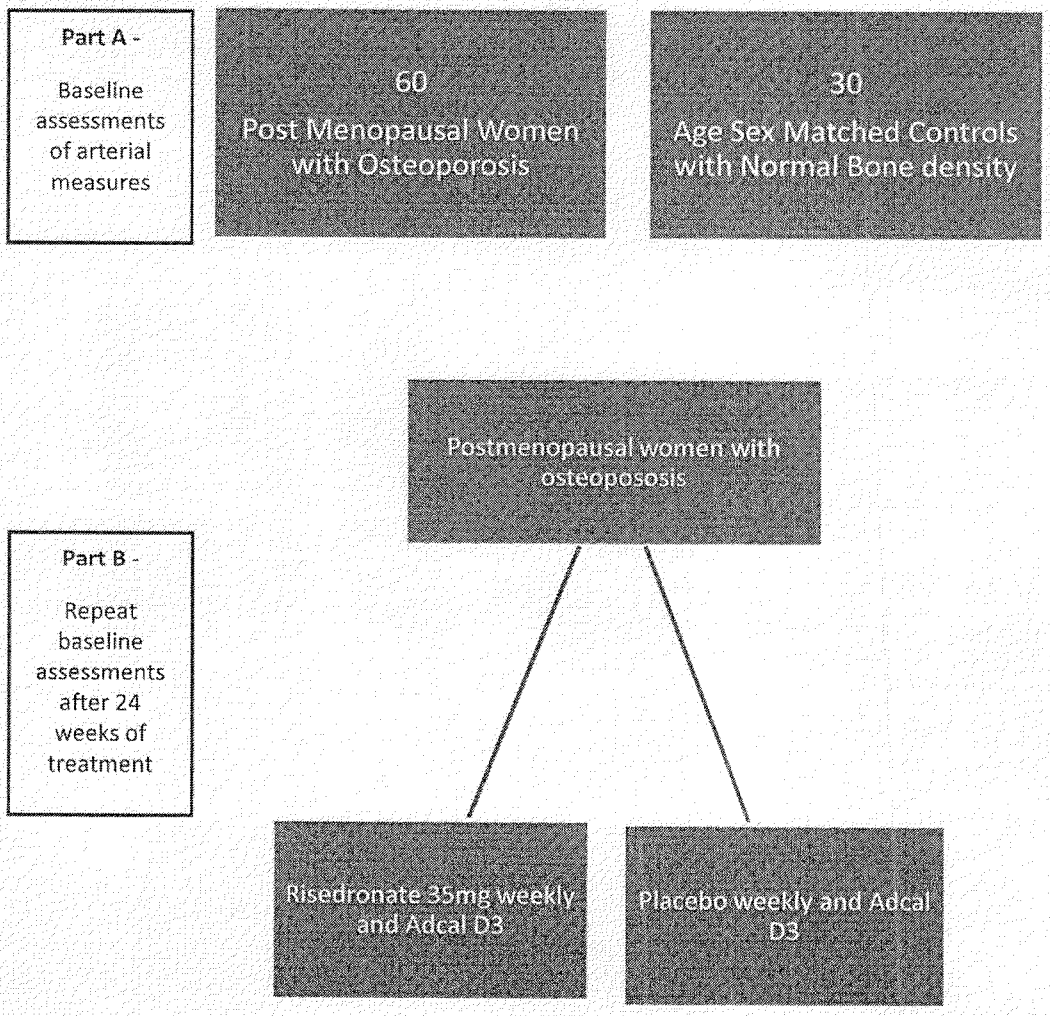
1. To examine endothelial function and vascular reactivity in patients with postmenopausal osteoporosis at global, local and microvascular levels

2. To examine platelet free radical generation (nitric oxide and superoxide) in postmenopausal osteoporosis.

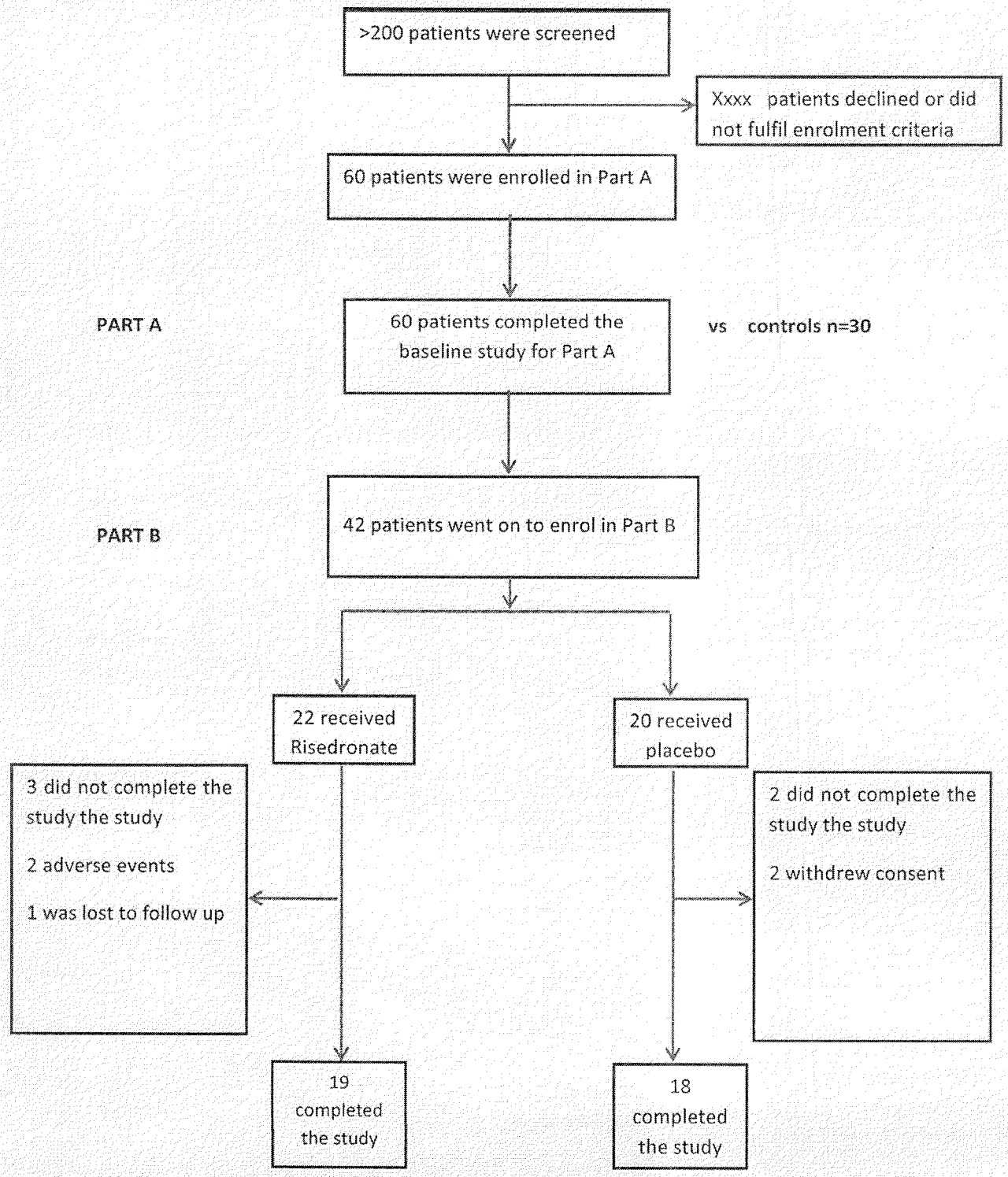
3. To employ the platelet as a compartmentalised model of endothelial function to study the activity of GTPase proteins in relation to free radical activity at baseline and after treatment with nitrogen containing bisphosphonates in post-menopausal women with osteoporosis.

4. To correlate these findings with serial biochemical markers of bone turnover as a measure of treatment efficacy and compliance

Study Design



Breakdown of the number of patients participating in the study



Statistical Analysis

The statistical analysis is currently being performed by a statistician in health statistics. To date preliminary results show no statistically significant differences in vascular measurements between placebo and Risedronate after 24 weeks of treatment. However there are some statistically significant differences between healthy controls and patients for baseline measures of vascular function.

Adverse Events

Routine adverse events included high cholesterol readings and high blood pressure readings. These results were fed back to both patients and GPs at the time of attendance. Serious adverse events were all unrelated to the IMP but were reported to the sponsor according to the correct protocols.

1. A patient recruited to the trial with a history of smoking was diagnosed with oesophageal cancer after reporting difficulty swallowing to her GP. This occurred within the first 3-4 weeks of enrolment after less than 4 treatment doses, she was referred by her GP for OGD and diagnosed with inoperable oesophageal cancer.
2. Two patients in the treatment arm withdrew, 1 due to excess wind and 1 due to fears about potential side-effects.
3. A patient was noted to have a thyroid nodule on scanning of her carotid artery. She was referred for FNA and although pathology was border line she proceeded to surgery for removal of the nodule.
   There were no SUSARS or SAEs that the sponsor deemed related to the IMP.

In total 30 healthy age and sex matched controls and 60 patients were recruited. Statistics show that both groups were equally matched in terms of age, blood pressure, and cholesterol profile. However the control group had a higher mean weight, BMI, and smoking history with more controls being non-smokers. Both groups were matched for aspirin, statin use.

T-scores

All patients had a diagnosis of osteoporosis with a T score ≤ -2.5 at least at one or more sites and all controls had normal bone density with a T score of > -1.0.

Report

control0patient1		T-score Hip	T score L spine
control	Mean	-0.379310	.051724
	Std. Deviation	.8077214	1.0193207

patient	Mean	-1.875000	-2.768333
	Std. Deviation	.6074746	.6212321

When the final results are available they will be disseminated to both patients and controls. Every effort will be made to publish results in a peer reviewed article.