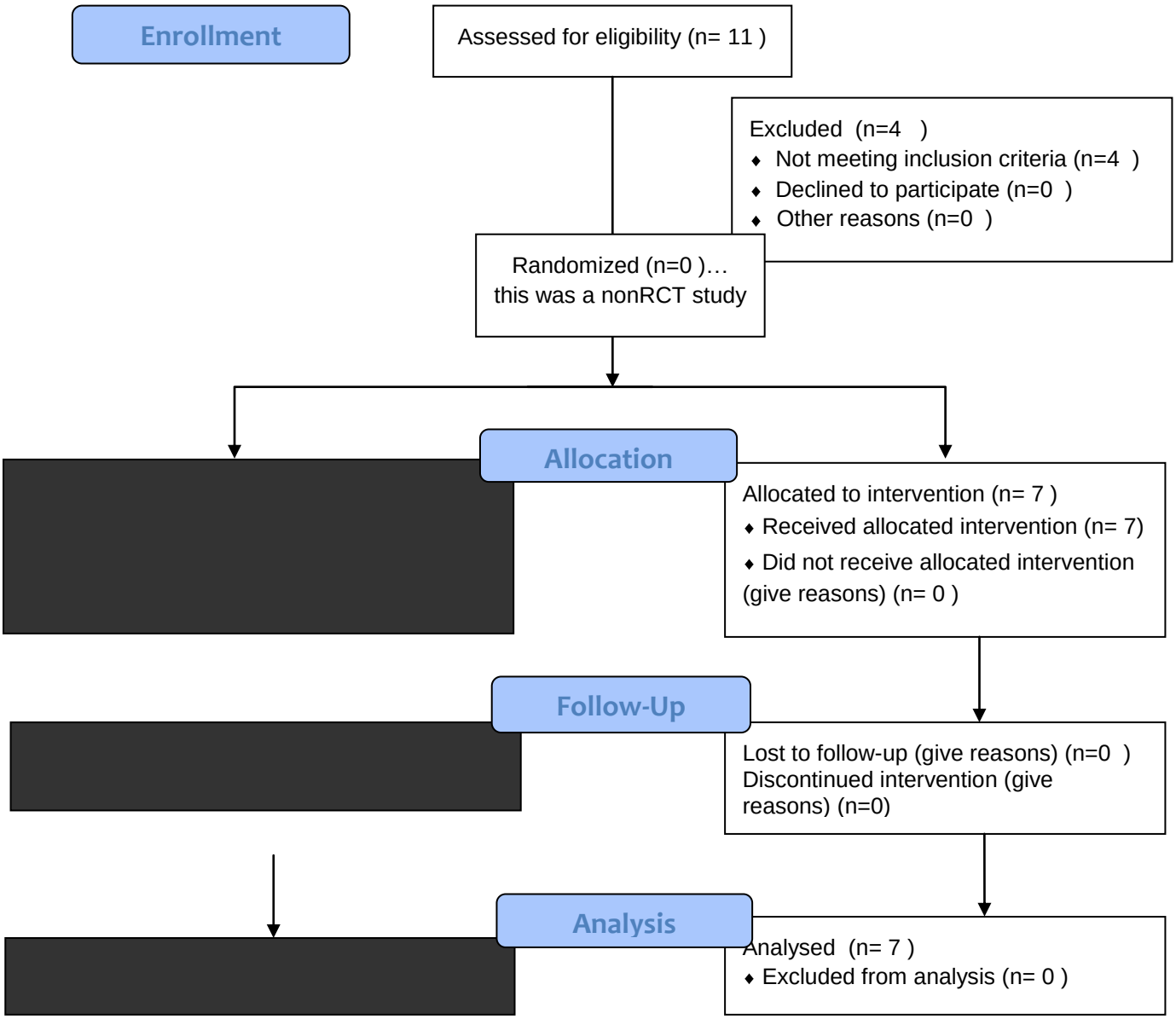
END OF TRIAL REPORT

Trial Identification and Report Information	
Title	An open label pilot study of Zoledronate (Aclasta 5mg iv) in the treatment of Ankylosing Spondylitis
Chief Investigator:	Professor JSH Gaston
EudraCT no.:	2007-000087-25
REC Ref no.:	07/HO305/54
R&D no.:	2005/182
Sponsor:	Cambridge University Hospitals NHS Foundation Trust
Sponsor's Address:	R&D Dept, CUHNHSFT, Hills Rd, Cambridge, CB2 0QQ
Trial Statistician:	none
Final Data Analysis carried out by:	Gavin Clunie, Amel Ginawi
Author of report:	Amel GINAWI (gavin CLUNIE)



Trial Summary	
Final Protocol version:	V01.3
Study Design:	An open label pilot study of Zoledronate (Aclasta 5mg iv) in the treatment of Ankylosing Spondylitis (AS). To establish whether Zoledronate (Aclasta 5mg iv) is likely to have a positive therapeutic effect on the inflammatory lesions of AS.
No. of participants:	Objective: 10 participants were planned to be treated though we were planning to screen up to 15 for eligibility; however, we recruited 11 and treated 7.
Investigational Medicinal Products:	Zoledronate (Aclasta 5mg iv in 100ml saline)
Date of End of Trial:	9th May 2011
Reported Serious Breaches:	*None*
Significant deviations identified during the trial:	None

Statistical Analysis and Main Findings	
Trial objectives and endpoints:	To record the change in inflammatory spinal skeletal lesions seen on magnetic resonance (MR) over 6 months following a single iv dose of Zoledronate (Aclasta) measured with Spine MR sparcc score spine at 6 months; secondary endpoints (clinical, lab at 3 and 6 months), BMD spine 12 months.
Trial Analysis Population:	4/11 were recruited, screened but not treated as they failed (protocol defined) eligibility criteria after baseline MRI. No changes in eligibility during the recruitment period
Statistical Methods:	Descriptive statistics used only because of low numbers – this was intended – see protocol Has the trial statistical methods changed during the trial? No.
Results:	Patients: Of eleven patients initially recruited, seven (6 male, 1 female; age range 35-54y) qualified for ZA treatment, with the other 4 patients failing to exhibit at least 2 scorable DVUs on the initial MR study. Baseline clinical data are shown in Table 1. No patients were being treated with disease modifying immunosuppressants. SPARCC MR imaging spinal inflammation scores: Baseline SPARCC scores

	ranged between 16-67 (of a maximum possible 108). Scores improved in 4/7 patients by 3 months after ZA treatment. All 4 patients' scores remained improved compared to baseline through to 6 months. At 6 months overall 6/7 patients had improved SPARCC scores compared with baseline (by 19-76%); see Table 2. Inter-rater reliability was good with the 2 observers' scores identical for 79% of DVUs and differing on 21%, in each case by a maximum of 1 only. Change in clinical features and indices: In the 6 months following treatment with ZA no patient had any change in therapy. All patients remained taking their NSAID regularly, there was no change in DMARD therapy and no patient was started on anti-TNFα therapy nor was treated with glucocorticoids. There was an improvement in mean BASDAI from the pre-treatment score of 6.3 to 5.3 at 3 months and to 5.1 at 6 months following ZA. Mean BASFI pre-ZA treatment was 6.0 and improved to 5.5 at 3 months and to 4.1 at 6 months. Mean MASES pre-treatment was 5.1 and mean score improved to 3.3 at 3 months and was 3.9 at 6 months.
Conclusion:	Although this is a small study, the results show that ZA treatment reduces the spinal inflammatory lesions of AS. The reduction in SPARCC scores over a 6-month period appears to mirror an overall clinical improvement in spinal symptoms, judged by pain scores and BASDAI over the same period of time. Six months might reasonably be considered a meaningful period of therapeutic response from a single treatment such as ZA. This is the first study in AS patients to report MR-defined change in spinal inflammatory lesions from ZA treatment. Because of small numbers of patients studied, we did not attempt to quantify any association between change in MR-defined SPARCC index and clinical indices. ZA treatment was tolerated well and there were no adverse events from the infusion. There is merit in considering further studies of ZA treatment in AS (and perhaps Axial Spondyloarthropathy). Further studies might reasonably be aimed at determining: whether there is clinical improvement when used for lesser severity AS; whether healthcare utilization and therapy 'needs' might be reduced or spared; if ZA has a role as adjunctive therapy (e.g. by randomized controlled trial 'add-on' therapy in anti-TNFα users). It will be important to determine whether clinical improvement occurs in association with, or independent from, the improvement in SPARCC inflammation (osteitis) scores in a larger series of patients.

Dissemination of Research Findings and Publications

To participants:	We will send participants a copy of the study write up together with a covering letter.
Publications:	*See also attached to email*

Chief Investigator's Signature	
	 Signature:_____ Date: 13th May 2013__