INTRODUCTION: Total hip arthroplasty (THA) is one of the most frequently performed orthopaedic operation with satisfactory results concerning mobility and life quality of the patients. In spite of continuous development of implant materials and surgical techniques, loosening of the implants and revision arthroplasty remain a major concern of this procedure. Periprosthetic bone loss is considered as a major factor in the loosening process, leading to destabilization and migration of the implant. Further it predisposes to periprosthetic fracture and makes any revision arthroplasty more difficult due to weak bone stock. The early diffuse periprosthetic bone loss is thought to be caused by altered bone strain and load conduction resulting in stress relief of proximal regions of femur with subsequent bone loss and by increased osteoclast-mediated bone resorption initiated by surgical procedure and damage to bony tissue. Follow-up dual x-ray absorptiometry (DEXA) measurements of periprosthetic bone mineral density (BMD) showed bone loss occurring mainly in the first few months after THA surgery and little changes after the first postoperative year. The present prospective double-blind study was designed to: 1) investigate if the inhibition of osteoclast-mediated bone resorption with alendronate, as a timely limited medication after surgery, can prevent the early periprosthetic bone loss and 2) determine dosis and duration of antiresorptive treatment needed.

METHODS: 51 patients (25 female and 26 male) with a mean age of 62.5 years (47 to 78; SD = 7.6), who underwent a unilateral THA with an unemented femoral stem, PPF® (Stratec, Umkirch, Germany), were assigned to placebo (n = 24) and alendronate (n = 27) treatment. The alendronate group was treated 2 months postoperatively with 20 mg/d oral alendronate. After 2 months the alendronate group was divided in 2 subgroups, one treated further 2 months (n = 13) and the other further 4 months (n = 14) with 10 mg/d oral alendronate. The indication for THA was degenerative primary osteoarthritis. Patients with accompanying diseases which were thought to influence the bone metabolism were excluded. The study was approved by the Institutional Review Board and all participants signed a consent form prior to the initial measurement.

The BMD of periprosthetic femur was measured 7 days postoperatively as reference baseline, followed by subsequent measurements 2, 4, 6, and 12 months postoperatively using dual-energy x-ray absorptiometry DEXA (Hologic® 4500 A, Waltham, USA). The protocol for analysis of the DEXA scans used radiological zones described by Gruen, regions of interest (ROI 1-7).

Biochemical markers of bone turnover were measured from serum separated blood collected in the morning of operation day between 0730 and 0800 a.m. and 2, 8, 16, 26 and 52 weeks after surgery. Bone specific alkaline phosphatase (Bone ALP, Metra™ BAP, QUIDEL, Heidelberg, Germany) and Osteocalcin (OC, N-MID® Osteocalcin One Step Kit, Nordic Bioscience Diagnostics A/S, Herlev, Denmark) were measured as markers of bone formation and C-terminal telopeptides of type-I collagen (CTX-I, Serum CrossLaps™ One Step ELISA, Osteometer BioTech A/S, Herlev, Denmark) as marker of bone resorption.

Changes in periprosthetic BMD and biochemical markers in follow-up measurements were expressed as mean percent loss or gain relative to the baseline reference at each scheduled time. The significance of the calculated data between scheduled times and baseline reference within a group was tested with Wilcoxon-test and between different groups with Mann-Whitney test. The threshold of significance was set at 0.05 (P-value).

RESULTS: One female patient of alendronate group discontinued the study after 3 weeks due to gastrointestinal complaint. 12 months after surgery patients in placebo showed significant loss of periprosthetic BMD in ROI 1, 2, 6 and 7 with greatest loss in ROI 7 (-7.3%, p = 0.02; -22.4%, p = 0.003 respectively) and those treated 6 months showed only a moderate BMD loss in ROI 7 (-10.2%, p = 0.05) and significant BMD gain in ROI 4 and 5 (7.4%, p = 0.002 and 6.9%, p = 0.01 respectively). The follow-up measurements revealed that BMD in ROI 6 and 7 in alendronate group treated 4 months did initially not decrease, but decreased continuously after 4th postoperative month achieving values of placebo group 12 months after surgery (Figure 1).

**Figure 1**: Changes of periprosthetic BMD in ROI 6

The bone resorption marker CTX-I increased moderately in placebo (17%, p = 0.04) with a peak at week 2. In both groups treated with alendronate CTX-I decreased over 100% (p = 0.001) over 6 postoperative months (Figure 2). The bone formation markers, bone ALP and osteocalcin increased in placebo up to 66% (p < 0.001) and 29% (p = 0.02) respectively with peak at week 26. In alendronate treatet group, bone ALP increased but in less extend than in placebo and osteocalcin remained constant at baseline value.

**Figure 2**: Postoperative course of bone resorption marker CTX-I

DISCUSSION: As investigated in many studies, the greatest periprosthetic bone loss occurs in proximal regions of femur particularly in ROI 7. In this study the treatment with alendronate 6 months postoperatively following THA reduced periprosthetic bone loss in ROI 7 significantly and prevented bone loss in other regions. With regard to the duration of antiresorptive therapy these data suggest that a minimum of 6 months treatment is needed to achieve a long term effect on periprosthetic BMD. The effect of alendronate on periprosthetic BMD is supported by demonstrated changes of biochemical bone marker. However, a longer duration of CTX-I suppression after surgery with 6 months treatment was expected. Whether prevention of periprosthetic BMD loss is of long-term effect or the long-term clinical outcome will be affected by limited postoperative antiresorptive therapy, are subjects of further investigation.