GLUCOSAMINE SULFATE THE FIRST PROVEN TREATMENT FOR DISEASE (STRUCTURE) MODIFICATION IN OA

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GLUCOSAMINE SULFATE THE FIRST PROVEN TREATMENT FOR DISEASE (STRUCTURE) MODIFICATION IN OSTEOARTHRITIS (SIARCZAN GLUKOZAMINY — PIERWSZA METODA LECZENIA CHOROBY ZWYRODNIENIOWEJ O DOWIEDZIONYM WPŁYWIE NA STRUKTURĘ STAWU)

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Introduction: The goal of pharmacological treatment of osteoarthritis (OA) is to control symptoms (pain and limitation of function) and possibly also to retard or stop joint deterioration progression. Therefore drugs for the treatment of OA are classified as symptom and structure modifying drugs in OA. Several clinical studies have proven glucosamine sulfate (GS) to relieve symptoms in OA. These

clinical and also preclinical results suggested that GS can influence the biology of joint structures. Glucosamine is an aminomonosaccharide occurring naturally in almost all human tissues, largely in proteoglycans of articular cartilage. The normal source of glucosamine is endogenous biosynthesis from glucose. Exogenous GS is the preferential source for proteoglycan biosynthesis. GS is consequently incorporated into proteoglycan molecules (1) and shows a special tropism for cartilaginous tissues (2). Also sulfate ions are essential glycosaminoglycan and proteoglycan synthesis contribute to the inhibition of cartilage degrading enzymes. Preclinical experiments: GS stimulates proteoglycan synthesis in human osteoarthritic chondroctyes in vitro (3,4,5) and decreases the metalloproteinases, stromelysin and collagenase (4,5,6). Glucosamine also inhibits compression catabolic changes in chondrocyte biosynthesis and gene expression in bovine articular chondroctyes (7). In rat articular chondrocyte cultures glucosamine prevented dosedependently the inhibitory effects of IL-1 (8). In vivo in animal OA models the in vitro results were confirmed and reflected in reduced cartilage destruction (9,10,11). Clinical proof: Encouraged by the favourable preclinical results with GS indicating a normalisation of OA dysregulated cartilage metabolism, two clinical long-term trials of 3 year duration were carried out to examine the effect of GS on the progression of knee OA joint structural changes and symptoms. In the studies 212 resp. 202 patients with knee OA (ACR criteria) were randomly assigned, in a double-blind fashion, to the continuous treatment with oral GS, 1500 mg once-a-day, or placebo for 3 years. Weight-bearing, antero-posterior radiographs of each knee were taken at enrolment and after 1 and 3 years in the first study, in the second study after 1, 2 standardising patient positioning years, radiographic procedure. In the first study total mean joint space width (JSW) of the medial compartment of the tibiofemoral joint was assessed by digital image analysis by a validated computerised algorithm, while in the second study

the minimum JSW of the narrowest medial joint space was measured visually by a 0.1 mm graduated magnifying glass. Symptoms were scored at each 4-month visit by the (total) WOMAC and Leguesne indices. The two groups were comparable for demographic and disease characteristics in both studies. the first study (12) the placebo-treated patients had an average joint space narrowing (JSN) of approximately 0.08-0.1 mm/year, while no JSN occurred in the GS group. A slight worsening in symptoms was evident at the end of the treatment with placebo, compared to the improvement observed after GS. In the second study (13) the 3-year JSN observed with placebo was approximately 0.2mm and was significantly higher than with GS for which like in the first study no JSN occurred in average. Symptoms improved in both groups, but significantly more with GS than with placebo. The improvement tended to be proportionally higher on the Lequesne index than on the WOMAC. Conclusions: The clinical results have shown that GS has disease modifying properties in OA by inhibiting further degeneration of articular cartilage. They also confirmed that the natural JSN in knee OA is slow but can be prevented by GS that also induces a significant symptom improvement.