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INTRA ARTICULAR INJECTIONS OF HYLAN GF-20 REDUCE TYPE II COLLAGEN DEGRADATION IN PATIENTS WITH KNEE OSTEOARTHRITIS: THE BIOVISCO STUDY

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BACKGROUND: Viscosupplementation (VS) by intra articular (IA) injection of hyaluronic acid (HA) is efficacious to reduce pain in patients with knee osteoarthritis (K-OA). However little is known on its effect on joint metabolism as well as on its possible structure modifying effect.

OBJECTIVES: To investigate the effect of VS on circulating OA biomarkers in patients with K-OA.Methods: Prospective open label study. 51 patients with unilateral symptomatic K-OA (ACR criteria; Kellgren-Lawrence grade I to IV) received an IA injection of 2mL of HA (hylan GF-20) IA injection on days (D) 1, 7, 14 and were followed 3 months. At D-15 patients were examined and X-rays were performed, in order to exclude patients with bilateral K-OA, or those with more than 3 OA joints including the target knee. From D-15 to D90 concomitant therapies were unchanged. Walking pain (WP) on VAS was obtained at each visit. Clinical response was defined as a WP decrease ≥20 mm between D1 and D90 (minimal clinically important improvement-MCII). Urine (U) and serum (S) samples were obtained, using a standardized procedure, 2 weeks before the first injection (D-15), then at D1 (1st injection), D30 and D90. S-C2C, S-Cartilage oligomeric protein (S-COMP), S-HA, S-CS846 epitope, S-type II collagen propeptide (S-PIICP) and U-type II collagen C telopeptide (CTX II/creatinin) were assayed. Variations over time for each biomarker were studied using Wilcoxon rank sum test.

RESULTS: 45 patients (mean age 57.7, mean BMI 26.7) were analyzed. Two were excluded because of major protocol deviation (corticosteroid IA injection at D30), 2 did not receive any injection and 2 were lost to follow up. At baseline there was no difference between ITT and per-protocol population. Between D-15 and D1 there was no significant difference for any biomarkers (all $p>0.05$), indicating a good reproducibility in S and U measurements and the absence of spontaneous variation over time. At D1 U-CTX II/creat was correlated with WP ($p=0.006$). Between D1 and D90: Mean (SD) WP decreased from 57.7 (15.4) to 29.3(22.9) mm ($p<0.0001$). No variation was found for any S-biomarker. By contrast U-CTX II/creat was reduced by 20.5% and decreased significantly between D1 and D90 (385.1 vs 306.0 ng/mmol creat; $p= 0.02$). Otherwise U-CTX II level at baseline was predictive of clinical response to treatment (MCII) ($p=0.03$).

Conclusion: This study is the first one showing that 90 days after 3 hylan GF-20 IA injections the U-CTX II urinary levels significantly decrease compared to baseline, suggesting a slowdown of type II collagen degradation. Long term prospective trials are required to confirm this potential chondroprotective effect of HA.