

Hyaluronan derivative Hymovis® increases cartilage volume and type II collagen turnover in osteoarthritic knee: data from MOKHA study.

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OBJECTIVES

Intra-articular injections of hyaluronan represent one of the well-accepted standard of care for treating symptomatic knee osteoarthritis (OA). Until now, not much is known about the structural-modifying effect of this treatment justifying this open-label, prospective, multicenter, pilot study.

METHODS

46 patients with symptomatic knee OA received two treatment cycles of intra-articular injections (3 mL) of HYMOVIS® (8 mg/mL of hyaluronic acid hexadecylamide) at 6 months interval. Each treatment cycle involved two intra-articular injections one week apart. All patients had MRI of the target knee and blood samples to assess joint biomarkers.

RESULTS

Coll2-1 and PIIANP serum levels significantly increased overtime while Coll2-1NO2 levels were only increased at D360. Interestingly, the ratios Coll2-1/PIIANP and CTX-II/PIIANP decreased, indicating a decrease of cartilage catabolism (table 1).

Table 1: levels (mean (SD)) of soluble biomarkers in the Full Analysed Set Population

	D0	D90	D180	D210	D360
Coll2-1 (nM) p value	522.06 (267.07)	618.41(270.96) 0.021	683.52 (333.42) <0.01	678.77 (289.84) 0.01	689.73 (304.12) <0.001
Coll2-1NO2 (pg/ml) p value	447.30 (431.62)	411.35 (367.82) 0.907	396.60 (206.11) 0.225	458.48 (238.84) 0.272	544.48 (449.13) 0.027
CTX-II normalized (ug/mmol) P value	0.014 (0.009)	0.012 (0.006) 0.924	0.013 (0.007) 0.882	0.029 (0.090) 0.924	0.014 (0.008) 0.910
PIIANP (ng/ml) P value	672.75 (240.47)	733.55 (265.39) 0.038	801.74 (269.60) <0.01	901.74 (315.61) <0.001	1083.77(446.75) <0.001
Coll2-1(nM)/PIIANP (ng/ml) p value	0,799 (0.359)	0,935 (0.681) 0.677	0,864 (0.387) 0.257	0,798 (0.396) 0.678	0,643 (0.273) 0.005
CTX-II (ng/mmol)/PIIANP(ng/ml) p value	0,024 (0,020)	0,018 (0,011) 0.041	0,018 (0,010) <0.01	0,034 (0, 10) <0.01	0,013 (0,007) <0.001

Compared to baseline value, MRI cartilage volume and thickness increased in lateral femoral and trochlea compartments and not in medial compartments. T2 mapping score was improved and WORMS effusion score was significantly decreased (table 2). Finally, global KOOS score and subscales significantly increased overtime while pain at rest, walking pain and patients or investigators global assessment of disease activity decreased. The safety profile was favorable with a low incidence of injection-site pain.

Table 2: WORMS total score and by features (mean (SD)) in the Full Analysis Set population.

	D0	D180	D360
WORMS total score Change from baseline p value	63.95 (27.78)	64.39 (27.71) 0.38 (1.77) 0.183	64.08 (28.03) 0.96 (2.75) 0.037
Cartilage Change from baseline p value	23.83 (11.27)	23.01 (11.13) 0.18 (0.70) 0.188	23.03 (11.45) 0.45 (1.21) 0.025
Cyst Change from baseline p value	2.73 (2.65)	2.83 (2.65) 0.10 (0.30) 0.125	2.90 (2.62) 0.23 (0.63) 0.047
Effusion Change from baseline p value	0.93 (0.69)	0.76 (0.54) -0.17 (0.38) 0.016	0.77 (0.54) -0.15 (0.54) 0.148

CONCLUSION

HYMOVIS®, a well-tolerated intra-articular treatment, significantly enhanced type II collagen turnover as suggested by the increase in Coll2-1 and PIIANP levels and cartilage volume observed by MRI in lateral knee compartment. Importantly, this study highlighted the potential symptomatic benefit of HYMOVIS® on pain and function and provides critical information for the design of a larger phase III clinical trial.

