[2013] [OP0031] BASELINE MEASUREMENTS OF COLL2-1 AND COLL2-1NO2 IN URINE ARE HIGHLY PREDICTIVE OF JOINT SPACE NARROWING IN KNEE OSTEOARTHRITIS

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Background: Coll2-1 and Coll2-1NO$_2$are biomarkers of cartilage degradation. Coll2-1 is a peptide of 9 amino acids (^{108}HRGYPGLDG^{116}), located in the helical part of type II collagen molecule. Coll2-1NO$_2$ [HRGY(NO$_2$)PGLDG], the nitrated form of Coll2-1, is a marker of cartilage degradation related to inflammation.

Objectives: To evaluate the predictive value of Coll2-1 and Coll2-1NO$_2$ for radiographic knee osteoarthritis progression.

Methods: Coll2-1 and Coll2-1NO$_2$ were measured in 178 plasma (sColl2-1 and sColl2-1NO$_2$) and urine (uColl2-1 and uColl2-1NO$_2$) samples from obese women with moderate unilateral radiographic knee OA. Changes in joint space width (JSW) in the medial tibiofemoral compartment were obtained from fluoroscopically assisted semi-flexed AP radiographs performed at baseline and 30 months. Coll2-1 and Coll2-1NO$_2$ were measured at baseline and after 6, 12, 18, 24 and 30 months. Patients showing a decrease of JSW≥0.5 mm over 30 months follow-up were considered as radiographic progressors. The descriptive and predictive values of plasma and urinary biomarkers were determined by univariate and multivariate data analysis at several time points. Throughout these analyses, we have been mainly interested in the feasibility and design of really predictive solutions. To assess the predictive power of the markers, resampling strategies were set up where a randomly drawn sample of patients was used to build a predictive model (a regularized logistic regression), while the patients not used to build this model were used to validate its predictive performance. This scheme was repeated several hundreds of time.

Results: The 178 women were, on average, 53.88 years old and had a BMI of 36.14kg/m^2. The minimum JSW at inclusion was 3.94 mm (3.17 mm- 4.55 mm) [median (interquartile range)]. After 30 months, the minimum JSN was -0.53 mm (-0.91 mm- -0.15 mm). Among this population, 86 patients were radiographic nonprogressors while 92 patients were radiographic progressors. When the discrimination power of a single marker at a single time point was studied, only the difference between M18 and M0 of uColl2-1 tended to reach the signification (p= 0.052, with p-values corrected for multiple testing). As far as predictive power in terms of AUC is concerned, similar solutions based on only one out of the two biomarkers have been built. The best AUC obtained were for uColl2-1NO$_2$ at M0 and uColl2-1 at M0 and M6 and M0 and M18. When combining several biomarkers at several time-points, equivalent solutions have been built for M0&M6, M0&M18 but also for M0 only. The results obtained are summarized in table 1

Table 1: Area under the curve for single biomarker at multiple time-points and for combination of biomarkers at multiple time-points

	Coll2-1		**Coll2-1NO$_2$**		**Coll2-1&Coll2-1NO$_2$**
	Urine	Plasma	Urine	Plasma	Urine
M0	0.57	0.53	0.61	0.48	0.66
M0&M6	0.65	0.59	0.59	0.59	0.66
M0&M18	0.62	0.54	0.58	0.60	0.70

Conclusions: Some interesting results were obtained with plasma but all the best results were obtained in urine. Out of the 2 biomarkers, Coll2-1 provided the best performance when taken at baseline. M6 and M18 time-points in urine could be considered as equivalently predictive. Nevertheless, a combination of both biomarkers in urine provided a gain in predictive performance (AUC up to 0.70).

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