The main outcomes were knee structural changes including the loss of Glu and CS.

Results: Participants reported taking (−) (n=300) or not taking (−) (n=300) OA treatment (analgesics/NSAIDs) over 24 months, with or without Glu/CS. The participants with meniscal extrusion had more knee OA structural damage at baseline and more knee OA progression as assessed by both X-rays and qMRI. Patients in both - and + analgesics/NSAIDs groups with meniscal extrusion had significantly greater cartilage volume loss in the medial compartment compared to those without meniscal extrusion.

No significant effect on JSW loss was found at T24 between - and + analgesics/NSAIDs groups, regardless of the presence or absence of meniscal extrusion and of the consumption or not of Glu/CS, whereas significant differences emerged for cartilage volume loss when examined by qMRI.

In the + analgesics/NSAIDs group (mild disease) with meniscal extrusion (more progressive disease) participants taking Glu/CS had less cartilage volume loss in the plateau (p=0.01). Multivariate analyses further confirmed in the + analgesics/NSAIDs group, that those with meniscal extrusion who took Glu/CS had significantly less cartilage volume loss in the medial plateau (p=0.009).

In the + analgesics/NSAIDs group, at T24, participants without meniscal extrusion (moderate disease) taking Glu/CS had less cartilage volume loss in the global (p<0.002, univariate and multivariate analyses) and medial and lateral plateau (p=0.034, p=0.013, respectively, multivariate analysis). However, in participants with meniscal extrusion (severe disease), although those taking Glu/CS had significantly less cartilage volume loss in the medial condyle at T24 in univariate analysis, this finding was not confirmed in multivariate analysis.

Conclusions: The presence of meniscal extrusion is an important factor that can influence the drug effect on cartilage volume. X-rays were found to be much more sensitive than MRI at documenting the protective effect of treatment on structural changes. Indeed, with qMRI, the non-effect of Glu/CS on patients without meniscal extrusion not taking analgesics/NSAIDs, representing very mild disease, probably reflects that the cartilage volume loss was small and unlikely to provide an accurate estimate. Moreover, in subjects with meniscal extrusion who took analgesics/NSAIDs (severe disease), the non-effect observed likely reflects irreversible cartilage damage.

This study confirms that combined administration of Glu/CS has a significant beneficial effect at delaying knee OA cartilage volume loss in subjects with mild to moderate disease severity.

![Figure 1: Effects of Glu/CS at 24 months in - analgesics/NSAIDs group](image1)

![Figure 2: Effects of Glu/CS at 24 months in + analgesics/NSAIDs group](image2)