Disease Modifying Drugs for OA: from research to clinical evidence

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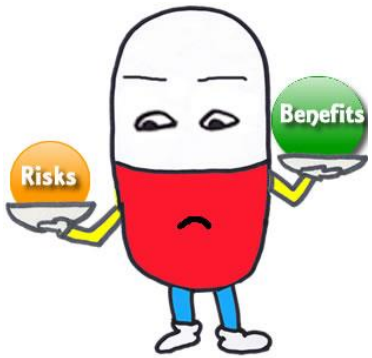
OA treatments and limitations



Intraarticular steroids, viscosupplements (GAG), topical NSAIDs, DMOAD (GAG)

	Limitations
Surgery	Costly, invasive procedure Primarily indicated for «end stage » OA
Prescription NSAIDs Including COXIB	GI bleeding or other complications CV risks Renalr complications
OTC NSAIDs	GI bleeding or other complications CV risks Renal complications
Acetaminophen	Hepatotoxicity
Patient education, physical and occupational Therapy, weight loss	Poor patient compliance

Modified Clegg et al. Eur J Orthop Surg Traumatol, 2013

What's a DMOAD?

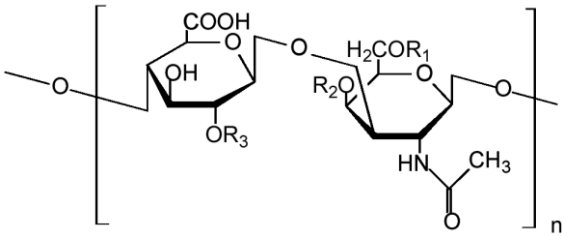
Disease-Osteoarthritis Modifying Drugs (DMOAD) is a category of otherwise unrelated drugs defined by their use in OA to slow-down disease progression

Primary outcome

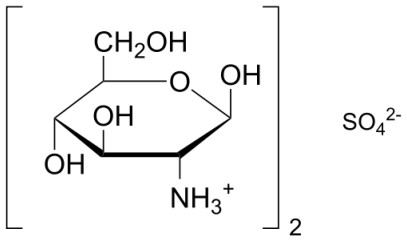
-Joint space narrowing
- MRI (volume)
-Time to surgery
- Number of prothesis

Most popular candidate

-Glucosamine (GlcN) S or HCL
-Chondroïtin sulfate (CS)
-Unsaponifiable of Soybean/Avocado (ASU)
-Diacerein

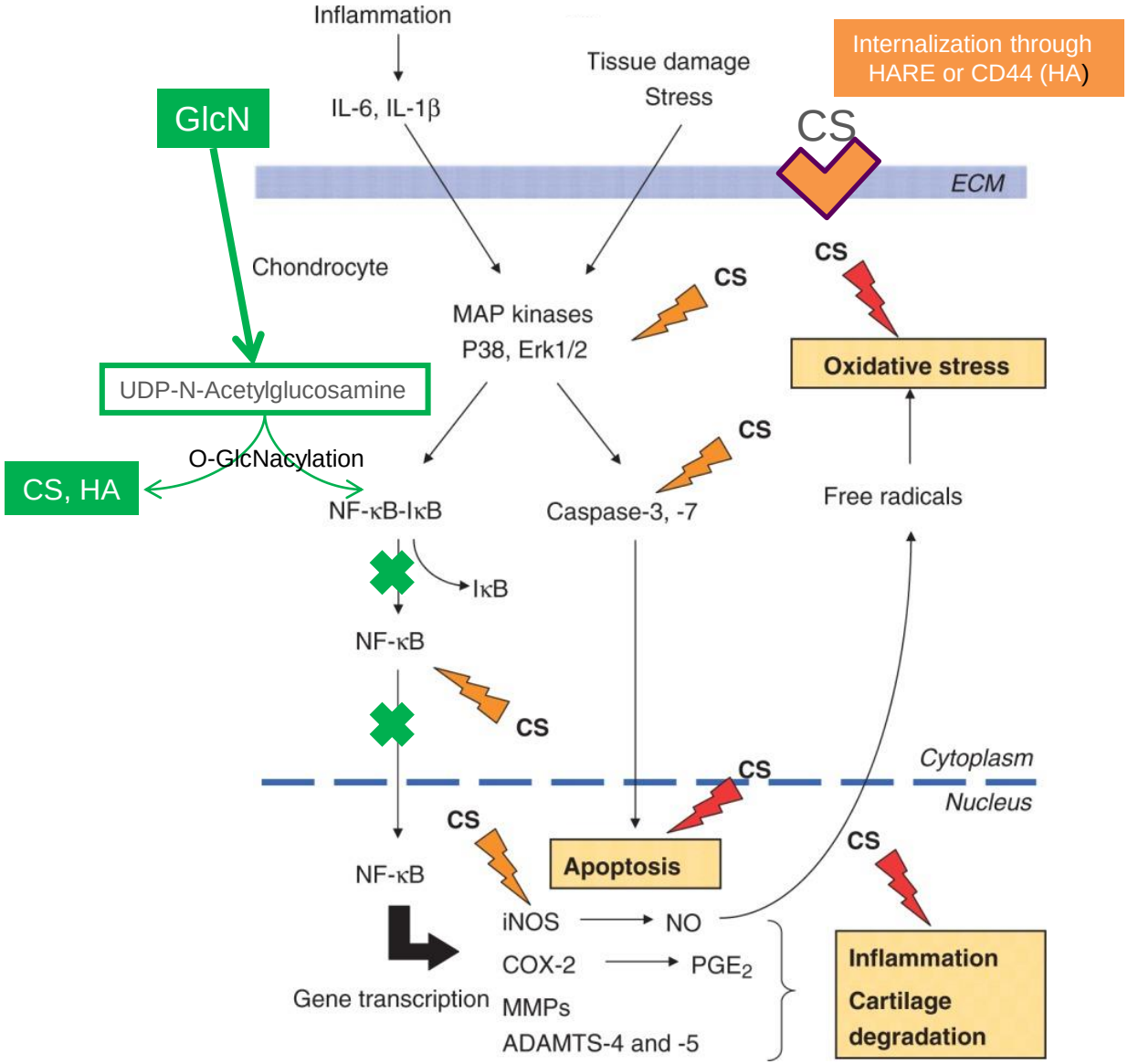


Chondroitin sulfate



Glucosamine sulfate/HCL

CS/GlcN: How do they work?



Henrotin et al. Ther Adv Musc Dis, 2010

GLcN/CS has a moderate effect on knee OA symptoms

OARSI meta-analysis

(Zhang et al, 2010)

	ES Pain	ES Function
Acetominophen	0.14 (0.05,0.23)	0.09 (-0.03,0.22)
Diacerein	0.24 (0.08, 0.39)	0.14 (0.03, 0.26)
NSAIDs	**0.29 (0.22,0.35)**	**-**
Aerobic	0.52 (0.34; 0.70)	0.46 (0.25, 067)
Glucosamine Sulfate	0.58 (0,30, 0.87)	0.07 (-0.08,0,021)
Chondroitin sulfate	0.75 (0.50, 1.01)	-

*All Studies

ES < 0.2 = None
ES 0.2 – 05 = Weak
ES 0.5 – 08 = Moderate
ES > 08 = Strong

versus placebo at 1-4 weeks

GAG effect size is superior to NSAIDs with less GI adverse events

GLcN/CS have a weak effect on disease modification

- **Chondroitin sulfate**

  Estimated Effect Size for reduction in rate of decline of minimum joint-space width (SMD): Ranges from 0.26 (0.14–0.38) to 0.30 (0.00–0.59) WEAK

- **Glucosamine sulfate**

  Estimated Effect Size for reduction in rate of decline of minimum joint-space width (SMD): 0.08 (−0.12–0.27) NONE

McAlindon et al. O&C 2014

Rationale to use GlcN or CS in OA treatment?

- Level of evidence : strong
- Quality of evidence: good
- Analgesic effect: moderate (> NSAIDS or Acetaminophen)
- Disease-modifying effect: None to weak (possible deleterious effect of NSAIDS)
- Safety : good (Severe adverse effect with NSAIDs)

BUT……

GLcN/CS in Recent Guidelines

Society	recommendation
ACR 2012	Conditionally recommend that the patients with knee or hip OA should not use chondroitin sulfate or glucosamine
NICE 2013	Nutraceuticals: do not offer glucosamine and chondroitin products for the management of OA
OARSI 2014	« Uncertain » for symptoms relief « Inappropriate » for structural effects

Why this reluctance for DMOAD?

- Lack of confidence in clinical trial?
- Geographical different practice?
- Inconsistency between industry-sponsored and independent studies?
- Heterogeneity among studies?
- Gap between expert opinion and real life?
- Cost of the treatment? Economical concern?

The risk

« ….iatrogenesis due to the overuse NSAIDs, paracetamol and corticosteroids infiltration… »

Letter of the « Section arthrose » of the french society of rheumatology to CNEDIMTS

Conclusions

At least 2 good reasons to use DMOAD in OA:

- To control OA symptoms with a good safety
- To decrease NSAIDs consumption

But

- Evaluate DMOAD efficacy at individual level
- Stop treatment after 6 months if no clinical relevant pain effect

Bone and Cartilage Research Unit

Team

Thank you for your attention !

International collaborations:

F Blanco (La coruna, Spain)
T Conrozier (CHU Lyon, France)
V Kraus (Duke University, USA)
L Punzi (University of Padova, Italy)
A Mobasheri (University of Notttingham, UK)
J Monfort (Hospital del mare (Spain)
P Richette (Lariboisiere, France)