**Mandl LA, Wolfe S, Daluiski A, et al. A Randomized Controlled Trial of Hylan G-F 20 for the Treatment of Carpometacarpal Osteoarthritis. Arthritis Rheum 2012;64:S475–6.**

PMID: Not yet published

Clinicaltrials.gov identifier: NCT00398866

Design: Phase 3 randomized clinical trial

Purpose of study: to test the hypothesis that treating carpometacarpal osteoarthritis (CMC OA) with injectable hyaluronan results in greater pain relief and function than injection with corticosteroid or placebo in the form of a local anesthetic

Population/sample size/setting:

* 188 patients (127 women, 61 men, mean age 66.5) treated for osteoarthritis of the thumb at specialty hospitals in New York and Boston
* Inclusion criteria were:
	+ Presence of osteophytes or sclerosis at the carpometacarpal (CMC) joint
	+ Complaint of unacceptable pain despite modification of activity and a therapeutic dose of nonsteroidal anti-inflammatory drugs (NSAIDS), if tolerated
	+ If bilateral disease, only the most severely involved hand (as defined by the visual analog scale [VAS] for pain) will be entered in the study
	+ Able to follow instructions and complete questionnaires
	+ Failed conservative therapy with NSAIDS or COX-2 inhibitors
	+ Unable to tolerate COX-2 inhibitors
* Exclusion criteria were:
	+ Previous traumatic dislocation, ligament tear, or fracture of the thumb in the affected hand

Previous hand surgery on the affected hand

* + Known hand comorbidities (e.g., active carpal tunnel syndrome, de Quervains tenosynovitis, etc.)
* Systemic rheumatic disease
* Bleeding diatheses or anti-coagulation
* Allergies to steroids, chicken products, bupivacaine, or adhesive (e.g., double-sided tape)
* Current use of oral or intravenous steroids
* Active systemic malignancies
* Hyaluronan injection in the target CMC joint in the last 6 months
* Steroid or hyaluronan injection in any other joint in the last 6 months
* Insulin dependent diabetes mellitus (IDDM)
* Active infection
* Pain in the index joint that is more than 40 out of 100 on a VAS Pain scale
* End Stage CMC osteoarthritis, equivalent to bone on bone, Kellgren and Lawrence Stage IV
* Grade 3 or 4 Eaton and Litter (E+L) Classification
	+ E+L 3: Advanced joint distraction, subchondral cysts, and sclerosis
	+ E+L 4: Involvement of several joint surfaces

Interventions:

* Patients were randomized to two designated control interventions and one experimental intervention (n for each group not reported)
	+ 1 ml of bupivacaine 0.5% injected once a week for 2 weeks as control #1
	+ 1 ml (40mg) of triamcinolone (Kenalog) injected the first week, followed by a placebo injection of 1 ml 0.5% bupivacaine the second week as control #2
	+ 1 ml of hyaluronan (Synvisc) injected once a week for 2 consecutive weeks as the experimental intervention

Outcomes:

* Disabilities of the arm, shoulder, and hand outcome measure (DASH) measured during the first six months from the time of the intervention, designated as safety issue #1
* Pain VAS on a 100 point scale during the first six months, designated as safety issue #2
* Changes in DASH and in pain VAS were reported for 175 patients who continued in the study for six months
	+ DASH had no clinically meaningful improvement in any of the three groups at six months
		- Mean DASH for hyaluronan went from 28.8 at baseline to 26.1 at six months; for triamcinolone, the change was from 28.9 to 27.0, and for bupivacaine, the change was from 25.7 to 24.2
	+ Pain VAS did improve in a clinically meaningful amount in all three groups (by 10.1 points for hyaluronan, by 13.1 points for triamcinolone, and by 14.2 points for bupivacaine); there were no differences between treatment groups on this improvement
		- Pain VAS improved both for less advanced and for more advanced Kellgren and Lawrence grades, equally for all three interventions

Authors’ conclusions:

* In patients with CMC OA, intra-articular hyaluronan was not superior to corticosteroid or local anesthetic in reducing pain at 6 months; all three therapies produced equal benefit
* No clinically important benefit was produced in function as measured by the DASH in any of the intra-articular interventions

Comments:

* All information is extracted from an abstract published as a supplement to the journal *Arthritis and Rheumatism* in 2012, and from clinicaltrials.gov under the identifier listed above
* It appears that the study was intended for submission to the FDA for approval of the study drug as a treatment for CMC OA, and that it failed to meet the superiority to bupivacaine (the designated placebo intervention) in either endpoint
* There appears to have been a modification of the original study protocol, in that patients with K-L Grade IV were to have been excluded from participation; in fact, 88 of the 188 patients who entered the study were Grade IV
	+ None of the entries under “History of Changes” at the clinicaltrials.gov website indicates when the entry criteria were expanded
* Although the study was completed in March 2013, the clinicaltrials.gov website had no results reported as of Feb 5, 2016 (results are generally expected to be placed on the website within one year of completion)
* It is not clear whether the study will be published in a journal article (the author and principal investigatory has been contacted by e-mail)
* In spite of a lack of much information, the study appears to be a failed Phase 3 FDA trial for obtaining licensing of the drug for CMC OA, and its size is probably adequate to constitute evidence that hyaluronan is not effective for that condition

Assessment: Adequate for evidence that intra-articular hyaluronan is not superior to placebo for improving pain in the setting of carpometacarpal osteoarthritis, and that it does not improve function in a clinically important way in the first six months after injection