Highlights of a new publication on Efficacy and Safety of Diclofenac Sodium Gel (DSG 1%) in Hand Osteoarthritis

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Diclofenac Sodium Gel in Patients with Primary Hand Osteoarthritis: A Randomized, Double-blind, Placebo-controlled Study

Roy D. Altman, Renée-liliane Dreiser, Chester L. Fisher, Walter F. Chase, Donatus S. Dreher, and Josef Zacher

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Background

- Radiographic hand OA is prevalent in 55% while symptomatic hand OA is prevalent in around 7 to 26% of the elderly population
- Nonsteroidal anti-inflammatory drugs (NSAIDs) can reduce pain and improve function in hand OA. However, nonselective NSAIDs carry dose-related gastrointestinal (GI) risks, cardiovascular and renal adverse effects
- Topical NSAIDs provide effective analgesia but minimize systemic exposure, potentially reducing risk of adverse events. ACR guidelines conditionally recommended the use of topical NSAIDs in patients with hand OA[2]

Study Objective and Methodology

- Multicenter, 8-week, randomized, double-blind, placebo-controlled study
- To assess the efficacy and safety of topical diclofenac sodium 1% gel (DSG) in patients with symptomatic hand aged ≥ 40 years

Eligibility Criteria

Inclusion Criteria:

- Patients with OA pain in dominant hand for ≥ 12 months with use of NSAID for ≥ 1 pain episode
- Pain in dominant hand during the 24 hours before the baseline visit (rated as ≥ 40 mm on a 100-mm visual analog scale (VAS)), must exceed nondominant hand by ≥ 20 mm
- Patients taking NSAID at screening must have an increase in pain in the dominant hand of ≥ 15 mm during washout period (≥ 7 days) and posterior-anterior radiographs must show Kellgren-Lawrence grade 1, 2 or 3 changes in symptomatic joints

Exclusion Criteria:

- Exclusion criteria included Kellgren-Lawrence grade 4 OA, secondary OA, other rheumatic diseases, other painful nonrheumatic diseases or a diagnosis of fibromyalgia. Ambidextrous patients were also excluded

Study Design

Eligible patients were randomized in a 1:1 ratio to receive diclofenac sodium gel (Voltaren® Gel, N=198) or vehicle (N=187; 2g to each hand) four times daily for 8 weeks

Rescue medication (acetaminophen 500-mg tablets) was allowed to a maximum dose of 4g daily during washout and throughout double-blind treatment, excluding the 36 hours before each evaluation

Efficacy endpoints

3 coprimary efficacy indices selected before study initiation:

- OA pain intensity in the dominant hand during the previous 24 hours (100-mm VAS; 0 = no pain, 100 = unbearable pain)
- Total Australian/Canadian Osteoarthritis Hand Index (AUSCAN)* score for the dominant hand
- Global rating of disease activity (100-mm VAS; 0 = very good, 100 = very poor)

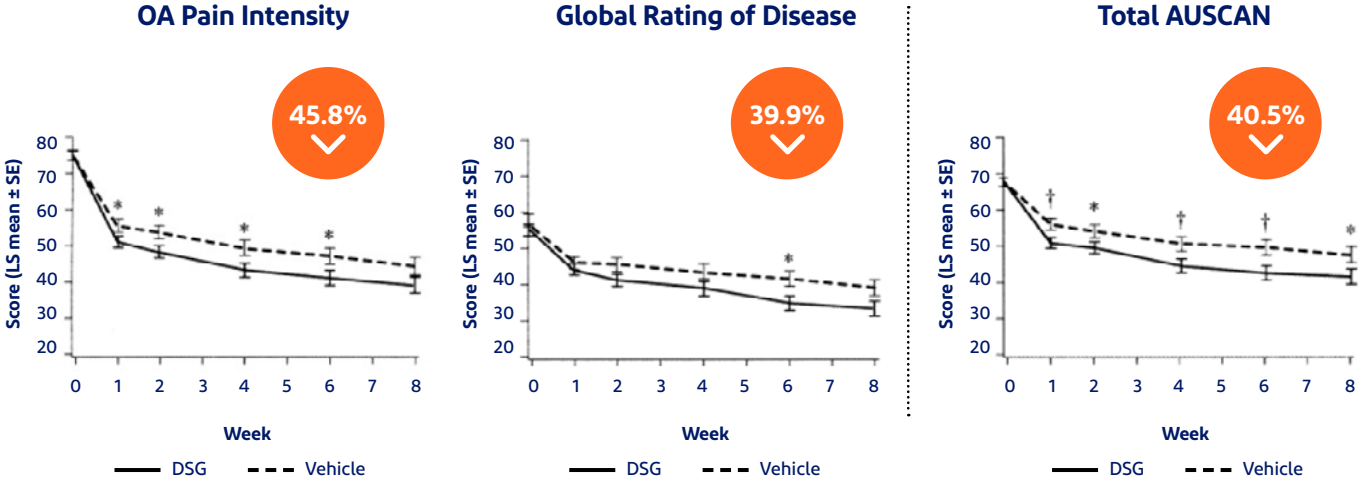
Primary endpoint	Secondary endpoint
4-week and 6-week measurements of: • OA pain intensity in the dominant hand during the previous 24 hours • Total AUSCAN score for dominant hand • Global rating of disease activity	• Measurement of 3 coprimary efficacy indices at Weeks 1, 2, and 8 • Measurements of pain, stiffness, and physical function subscales within AUSCAN index and OARSI* response at each visit

*The total AUSCAN score: the average of scores on 15 questions rating pain, stiffness, or function standardized to range from 0 (no pain/stiffness/difficulty) to 100 (extreme pain/stiffness/difficulty); The OARSI response: improvement ≥ 50% and an absolute change ≥ 20 mm in either pain or physical function, or as an improvement ≥ 20% and an absolute change ≥ 10 mm in ≥ 2 of the following: pain, patient global rating of disease, and physical function

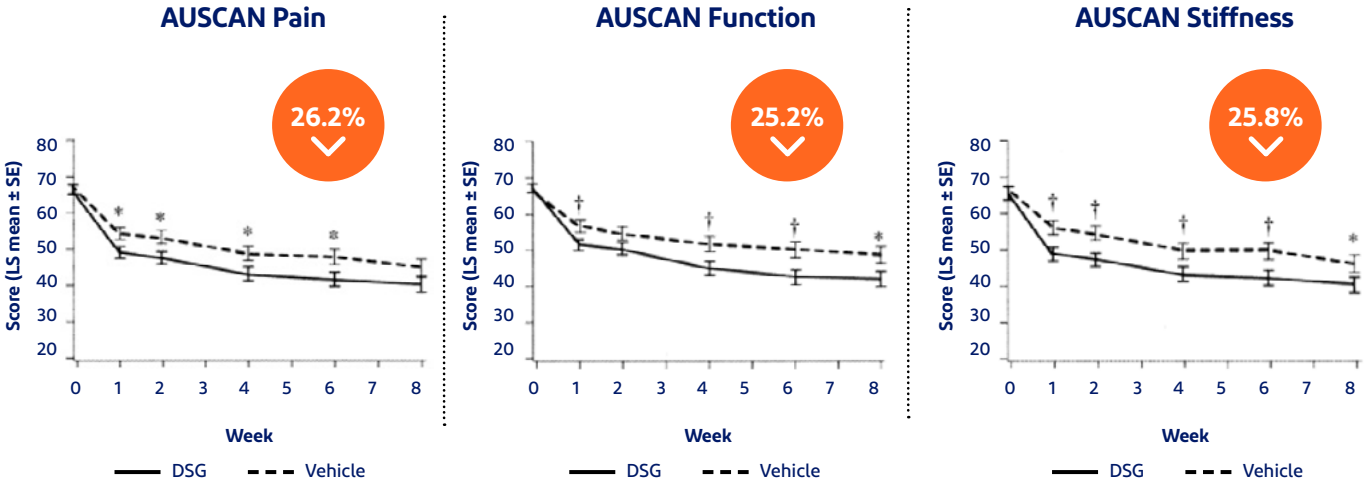
Results

Primary endpoints:

- At Week 4, DSG was significantly superior to vehicle on VAS pain, total AUSCAN but not on global rating of disease. DSG treatment reduced mean VAS pain intensity by 42.3% (31.1 mm, P=0.018), total AUSCAN score by 35.0% (23.5 mm, P=0.011) and global rating of disease by 36.1% (20.8 mm, P=0.06)
- In the vehicle group, reductions in mean VAS pain intensity, in total AUSCAN, and global rating of disease were 30.1% (23.9 mm), 39.9% (16.8 mm) and 40.5% (14.8 mm) lower, respectively, than in the DSG group
- At Week 6, DSG was significantly superior to vehicle in all primary outcome measures. DSG reduced mean VAS pain intensity by 45.8% (33.7 mm, P=0.023), total AUSCAN score by 38.5% (25.9 mm, P=0.006), and global rating of disease by 40.1% (23.1 mm, P=0.023) compared with baseline



- At Weeks 4 and 6, DSG was significantly superior to vehicle on each of the 3 AUSCAN indices. At week 4 and 6, DSG reduced pain, stiffness and function index to 24.1 mm (P=0.027), 23.4 mm (P=0.011), 23.2 mm (P=0.01) and 26.2 mm (P=0.021), 25.2 mm (P=0.005) and 25.8 mm (P=0.005), respectively when compared to baseline
- At Week 8, DSG remained significantly superior to vehicle on the AUSCAN stiffness (P<0.048) and functional (P<0.017) indices and was numerically superior to vehicle on the pain index (P<0.09)



Other efficacy measures:

- 47.7% of patients treated with DSG rated treatment 'Very Good' or 'Excellent' compared to 36.5% in the vehicle group
- Compliance with treatment for >6 weeks was similar in the DSG (77.8%) and vehicle (75.9%) groups
- Most patients (58.6% DSG, 57.8% vehicle) were compliant for all 8 weeks
- 82.1% of trial participants in DSG used rescue medicine (acetaminophen) vs 82.6% in the vehicle group

Secondary endpoint

- The proportion of OARSI responders in the DSG group increased steadily from 55.6% at Week 1 to 65.7% at Week 8 and was about 10% higher than the proportion of responders in the vehicle group
- For OA pain intensity in the nondominant hand, DSG was significantly superior to vehicle at Weeks 1 and 6 ($P<0.05$)

Safety

- 52% of patients in the DSG group compared to 43.9% in the vehicle group reported at least one treatment-emergent adverse event (AE), with most being of mild severity. The most common treatment emergent AE was headache, with 11.1% reported in the DSG group and 10.2% in the vehicle group
- Very few patients (2.5%, DSG; 2.1%, vehicle) experienced severe treatment-emergent AE
- The incidence of gastrointestinal (GI) adverse events was 7.6% in the DSG group and 3.7% in the vehicle group, with diarrhea being the most frequent GI AE. No ulcers or GI bleeding were reported

Study strengths

- This study provides evidence that diclofenac sodium gel is safe and effective in the management of primary hand OA over a period of 8 weeks and is consistent with the recommendations from EULAR and OARSI
- From week 1 till week 6, DSG showed superiority over vehicle on most primary and secondary Endpoints, with a peak at week 6

Conclusion

- Topical diclofenac sodium gel was generally well tolerated and effective in primary hand OA
- Improvements in the DSG group (16%–25%) were 47% to 125% greater than the vehicle group at Weeks 1 through 6, and 21% greater at Week 8

References

1. Altman, R. D., Dreiser, R. L., Fisher, C. L., Chase, W. F., Dreher, D. S., & Zacher, J. (2009). Diclofenac sodium gel in patients with primary hand osteoarthritis: a randomized, double-blind, placebo-controlled trial. The Journal of rheumatology, 36(9), 1991-1999.
2. Kolasinski, S. L., Neogi, T., Hochberg, M. C., Oatis, C., Guyatt, G.,Block, J., ... & Reston, J. (2020). 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis & rheumatology, 72(2), 220-233.