Methods: This was a double-blind, active control study. 244 healthy volunteers completed the study. Upper GI endoscopy was performed prior to and on day 14 after commencing treatment with naproxen (550 mg twice daily) or ATB-346 (250 mg once daily in the morning and placebo once daily in the evening). Whole blood thromboxane synthesis (COX activity) and plasma hydrogen sulfide levels were also measured.
Results: For the primary endpoint, incidence of ulcers ≥3 mm in diameter, 53 subjects (42%) taking naproxen developed at least one ulcer, while only 3 subjects taking ATB-346 developed at least one ulcer ($p<0.00001$). The two drugs produced comparable suppression of systemic COX activity. Subjects in the naproxen group developed more ulcers per subject (an average of 4) than in the ATB-346 group (1.3/subject), and a greater incidence of larger (≥5 mm diameter) ulcers (125 vs. 0), respectively. The incidence of abdominal pain, gastro-esophageal reflux and nausea were markedly lower with ATB-346 than with naproxen. Systemic COX activity was inhibited by 95% in both groups, and plasma H_2S levels were significantly elevated in subjects treated with ATB-346 (by ~50%; $p<0.001$).
Conclusions: As in pre-clinical studies, this phase 2 clinical trial demonstrated a dramatic increase in the GI safety of ATB-346 versus one of the most commonly used NSAIDs, naproxen. ATB-346 produced equivalent suppression of COX to naproxen, consistent with a previous Phase 2A clinical trial that demonstrated significant pain relief in patients with osteoarthritis of the knee. ATB-346 appear to be an effective and much safer alternative to existing NSAIDs.

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EFFICACY AND SAFETY FROM A PHASE 2B TRIAL OF SM04690, A NOVEL, INTRA-ARTICULAR WNT PATHWAY INHIBITOR FOR THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE

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Objectives: A phase 2a study of SM04690, a small-molecule, intra-articular (IA) Wnt pathway inhibitor reduced knee pain and improved physical function and medial joint space width (mJSW) at 52 weeks in subgroups of subjects with unilateral symptomatic knee osteoarthritis (OA) compared to placebo (PBO).[1]

A 24-week phase 2b study was conducted to refine patient reported outcome (PRO) measures, target population, medication dose, and to evaluate safety. PRO results for Weeks 12 and 24 are presented here.
Methods: Study subject inclusion criteria required ACR-defined knee OA, Kellgren-Lawrence (KL) grade 2 or 3, and Pain Numeric Rating Scale (NRS) scores ≥4 and ≤8 in the target knee and <4 in the contralateral knee. A single IA injection of 2 mL SM04690 (0.03, 0.07, 0.15, or 0.23 mg), vehicle PBO, or sham (dry needle only) was given in the target knee at baseline. PRO endpoints included change from baseline in weekly average of daily pain in the target knee by NRS diary (NRS) [0-10], Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Physical Function [0-100], and Patient Global Assessment (PTGA) [0-100]. Differences between active treatment groups and vehicle PBO were analyzed with baseline-adjusted analysis of covariance (ANCOVA).
Results: 695 subjects (mean age 59.0 [±8.5] years, BMI 29.0 [±4.0] kg/m2, female 58.4%, KL3 57.3%) were enrolled and dosed; 635 subjects (91.4%) completed the study. No meaningful differences in the incidence of adverse events were observed between treatment and control groups.

In the Full Analysis Set, significant improvements from baseline compared to vehicle PBO were observed in pain NRS for 0.07 mg (Week 12 [P=0.001], Week 24 [P=0.031]) and 0.23 mg (Week 12 [P=0.012], Week 24 [P=0.022]) SM04690 dose groups. Similar improvements were observed in WOMAC Pain for 0.07 mg (Week 12 [P=0.04]) and 0.23 mg (Week 12 [P=0.003], Week 24 [P=0.031]) dose groups. For WOMAC Physical Function, improvements were observed for 0.07 mg (Week 12 [p=0.021]) and 0.23 mg (Week 12 [p=0.006], Week 24 [P=0.017]) dose groups. PTGA improvements were observed for 0.07 mg (Week 12 [P=0.031]) and 0.23 mg (Week 12 [P=0.010], Week 24 [P=0.033]) dose groups.
Conclusions: SM04690, in development as a potential disease-modifying OA drug, showed in this Phase 2b study statistically significant improvements from baseline in both the 0.07 mg and 0.23 mg dose groups compared to vehicle PBO for Pain NRS, WOMAC Pain, WOMAC Physical Function, and PTGA. These data support the continued development of SM04690 as a treatment for knee OA. Phase 3 studies are being planned.

References

1. Yazici Y, et al. Arthritis Rheumatol. 2017; 69 (suppl 10).

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GIANT CELL ARTERITIS. TREATMENT WITH TOCILIZUMAB

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Objectives: Tocilizumab (TCZ) has shown efficacy in clinical trials and in real-world data on giant cell arteritis (GCA). We describe our experience with TCZ in GCA in those patients with inefficacy to previous therapies in a tertiary hospital.
Methods: Search and review clinical data of patients diagnosed with GCA and treated with TCZ in the last 5 years.
Results: 23 patients (3 men); mean age 71.5 (7.8). 57% positive temporal artery biopsy. 74% received treatment with sDMARD. 26% started TCZ in combination with methotrexate. Before TCZ was started, the median methotrexate and steroids doses were 20 mg (10-23.75) and 12.5 mg (5-30), respectively. 5 patients had visual lost: 2 amaurosis and 3 optic neuritis.

TCZ was started after a median time from GCA diagnosis of 12 months (2-21). Symptoms in all patients but one improved totally or partially; their CRP an ESR decreased to normal levels at month 1 ($p<0.0001$). 11/15 patients were asymptomatic at one year. 74% TCZ intravenously. We did not find different efficacy related to the administration route. 3 patients stopped TCZ: respiratory infection, lost of efficacy and hypertransaminasemia at 24, 18 and 2 months, respectively.

8 patients developed toxicity to steroids: 3 diabetes, 3 behavior alterations and 2 myopathies. Most relevant adverse side-effect was serious infections observed in 6/23.
Conclusions: In our series TCZ was effective, fast and safe treatment in the management of GCA refractory to other treatments.

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ASSESSMENT OF THE IMPACT OF CAPILLAROSCOPY TRAINING TO NON-EXPERT PROFESSIONALS AND ITS CORRELATION WITH EXPERT PROFESSIONALS IN NORTHWESTERN COLOMBIA, 2017

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Objectives: To evaluate the impact of a capillaroscopy training on non-expert professionals and its correlation with experience capillaroscopists in Medellín Colombia, 2017.
Methods: This study was quasi-experimental in its design and included individuals older than 18 who were medics or medical students and gave consent. Participants received a 30-minute introduction and were evaluated (time 1) with a test in which 60 photos were displayed for 30 seconds each. Participants were asked to assess the shape, size and general pattern of nail fold capillaries (20 photos in each section). Subsequently, a six-hour training was carried out, and a new evaluation was performed (time 2) with the same images as in time 1 but in a different order. The agreement among experts was considered the gold standard. The concordance between the experts (inter-reader, intra-reader) and the agreement of each participant with the expert at the two times were evaluated by the Kappa coefficient. The results obtained between the two times were compared using the Wilcoxon test.
Results: 56 medical professionals and two experts were included. The inter-reader and intra-reader agreement between the experts were substantial (Kappa between 0.61-0.80) and almost perfect (Kappa between 0.81-1.00), respectively. After the training, a significant increase was observed both in the number and in the percentage of correct answers with respect to the consensus of experts ($p<0.001$). The kappa coefficient for time 1 was: 0.50 (CI 0.33-0.71) for form, 0.76 (CI 0.53-0.79) for size, 0.45 (CI 0.29-0.57) for general pattern and 0.71 (CI 0.59-0.84) recognizing specifically scleroderma pattern. At time 2 the kappa was 0,80 (CI 0,60-0,90) for form, 0,76 (CI 0,55-0,80) for size, 0,64 (CI 0,46-0,79) for general pattern and 1 (CI: 1-1) for normal pattern vs systemic sclerosis.
Conclusions: A short Nailfold videocapillaroscopy training can improve the ability of non-expert personnel to identify capillaroscopic abnormalities. This is particularly important when recognizing the scleroderma pattern where the agreement with the gold standard was perfect.