**Evaluation of Outcomes in Osteoarthritis (OA) Patients Treated in the Arthrokinex Program at One Year**


## Abstract

**Objective:** The desired therapeutic effect of Arthrokinex is facilitated by the ability of IL-1-Ra to limit the destructive inflammatory intra-articular (IA) actions of IL-1β. A study published in the international journal Cytokine has proven the capacity of Arthrokinex to induce the anti-inflammatory cytokine, IL-1- Ra. The primary purpose of this ongoing osteoarthritis (OA) treatment program is to determine the ability of Arthrokinex conditioned serum to reduce pain, improve joint function and enhance quality of life in patients with knee, shoulder and hip osteoarthritis.

**Methods:** Venous blood from 164 patients currently enrolled in the Arthrokinex Joint Health Program with symptomatic osteoarthritis (knee, n=124; shoulder, n=20; hip, n=20) was conditioned and injected into the affected joint. Each patient received an ultrasound-guided IA injection each week for 3 consecutive weeks, followed by a maintenance injection every 3 months. Treatment outcome measures were assessed by three different patient-administered surveys at each visit. Using the Visual Analog pain Scale (VAS), participants were asked to classify pain in the previous 24 hours. The Extra Short Musculoskeletal Functional Assessment (XSMFA-D) survey is a series of 16 questions designed to determine the functionality of the OA-affected joint. Finally, the patient completed a patient global impression of change (PGIC) survey to assess their individual level of satisfaction with the treatment regimen.

**Results:** Data Analysis has been completed on 111 participants that provided data at the 3 month mark, 84 participants at the 6 month follow up and 73 participants at the 12 months follow up. The vast majority of patients (77%) reported a progressive and consistent reduction in knee ($p<0.0001$) and shoulder ($p=0.01$) pain 3 months following the initial IA injection of Arthrokinex. Hip pain was also reduced at the 3 month mark but did not reach statistical significance which can be attributed to the small sample size. Compared to baseline, a robust and statistically significant improvement in each XSMFA-D sub-scale was observed in knee OA patients after 3 months. Similarly, after 3 months, shoulder function significantly improved in three out of the four XSMFA-D categories. Hip function followed the same trend in overall function improvement after 3 months although not to a statistically significant degree. This overall reduction of pain and enhanced joint function was sustained for 6 months and even 12 months after the initial injection. A total of 74% reported better pain control at 6 months with 79% reporting improvement at 12 months. The statistically significant improvement in XSMFA-D categories also persisted after 6 and 12 months for knee and shoulder patients. In addition to symptomatic control of OA, 81% of patients reported satisfaction with the treatment regimen at 3 months, 90% at 6 months and 81% at 12 months after the initial injection.

**Conclusion:** Treatment of OA continues to be a challenge for clinicians and investigators. Given the limited scope and effectiveness of current treatment options aimed solely at symptomatic control of the disease, many patients are forced to undergo repeated steroid injections, chronically use NSAIDs/narcotics or undergo surgery. Given the favorable safety profile, reduction in pain and enhanced quality of life experienced by patients enrolled in this joint health program, Arthrokinex has the potential to offer an alternative, chondroprotective, natural, molecular approach to treating pain and functionality in patients with mild, moderate or severe Osteoarthritis.

ARTHROKINEX
JOINT HEALTH

# One Year Retrospective Clinical Outcomes for Arthrokinex ™

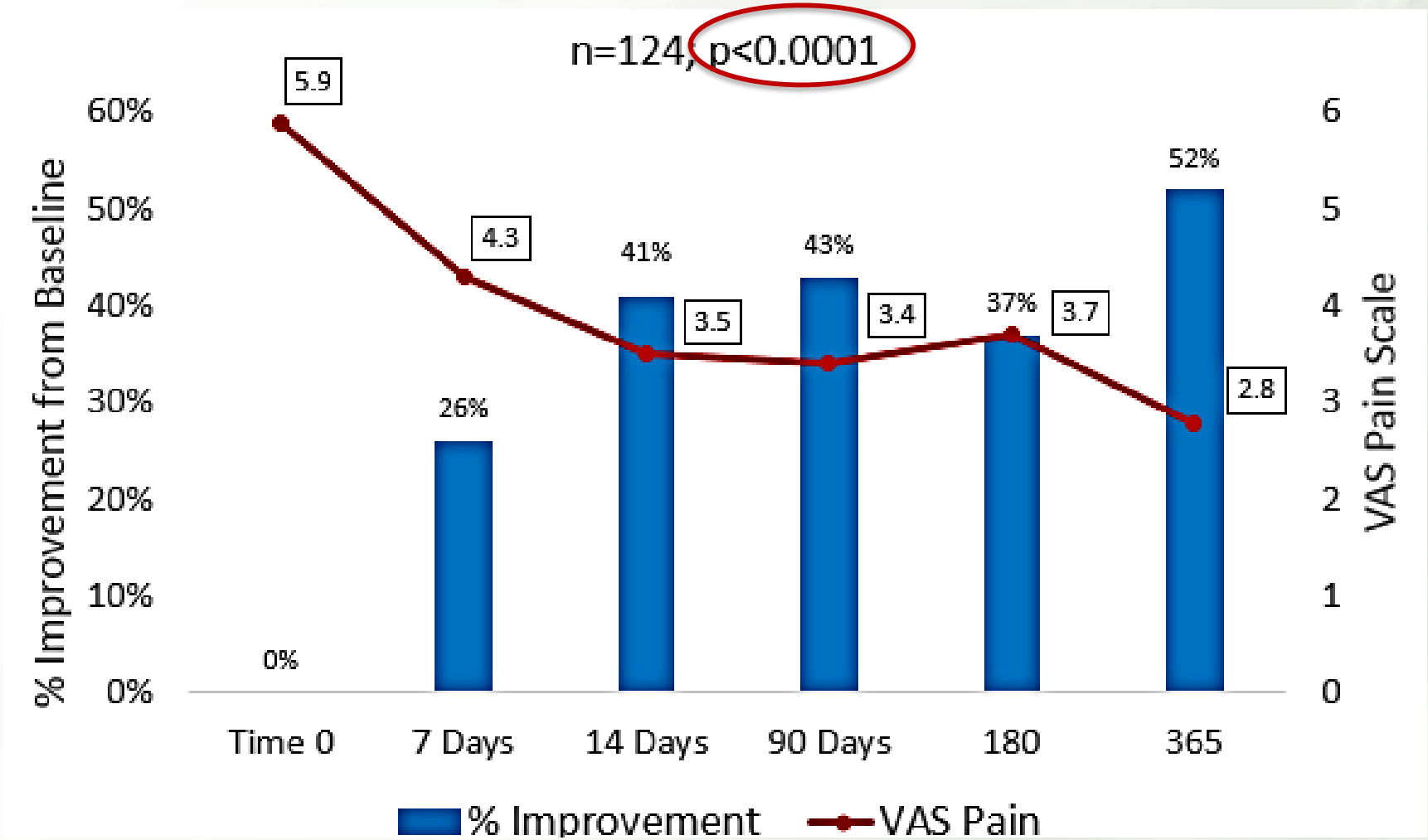
# One Year Retrospective Analysis of Arthrokinex™
## Study Overview

- This program involved 164 patients symptomatic osteoarthritis (knee, n=124; shoulder, n=20; hip, n=20) Approximately 40% of Arthrokinex ™ patients have moderate arthritis and approximately 60% have severe arthritis. Some patients have bone on bone
- Similar to the pilot program, each patient received a series of 3 Arthrokinex™ Joint Injections (Day 0, 7 and 14)
- VAS pain scores, Extra Short Musculoskeletal Functional Assessment (XSMFA-D) survey and Patient Global Impression of Change (PGIC) survey
- Outcome measures were analyzed by Wilcoxon signed rank tests to compare baseline values to data obtained at 12 months

# The Knee

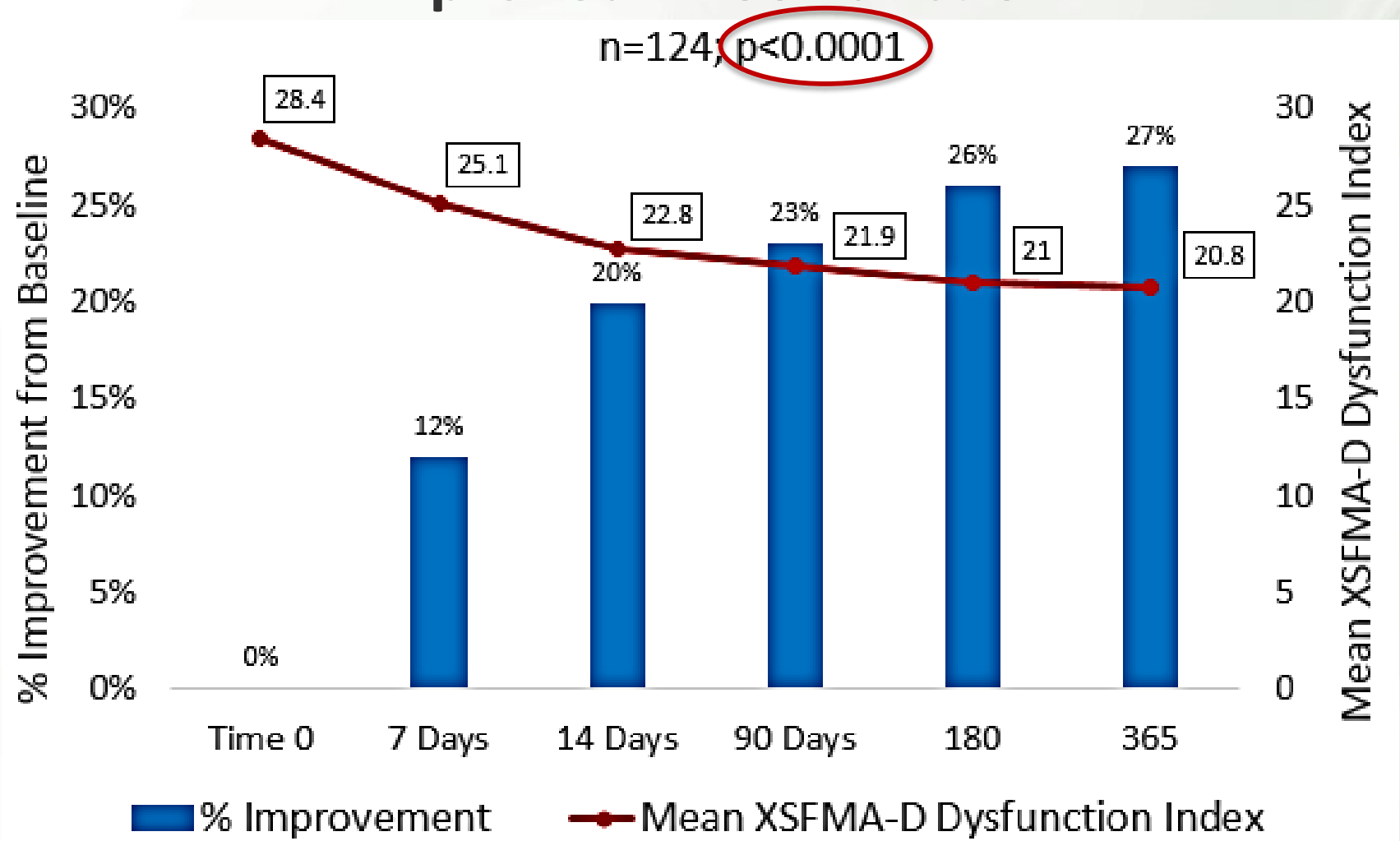
# Efficacy of Arthrokinex™ to Treat Knee OA

## Reduced Knee Pain



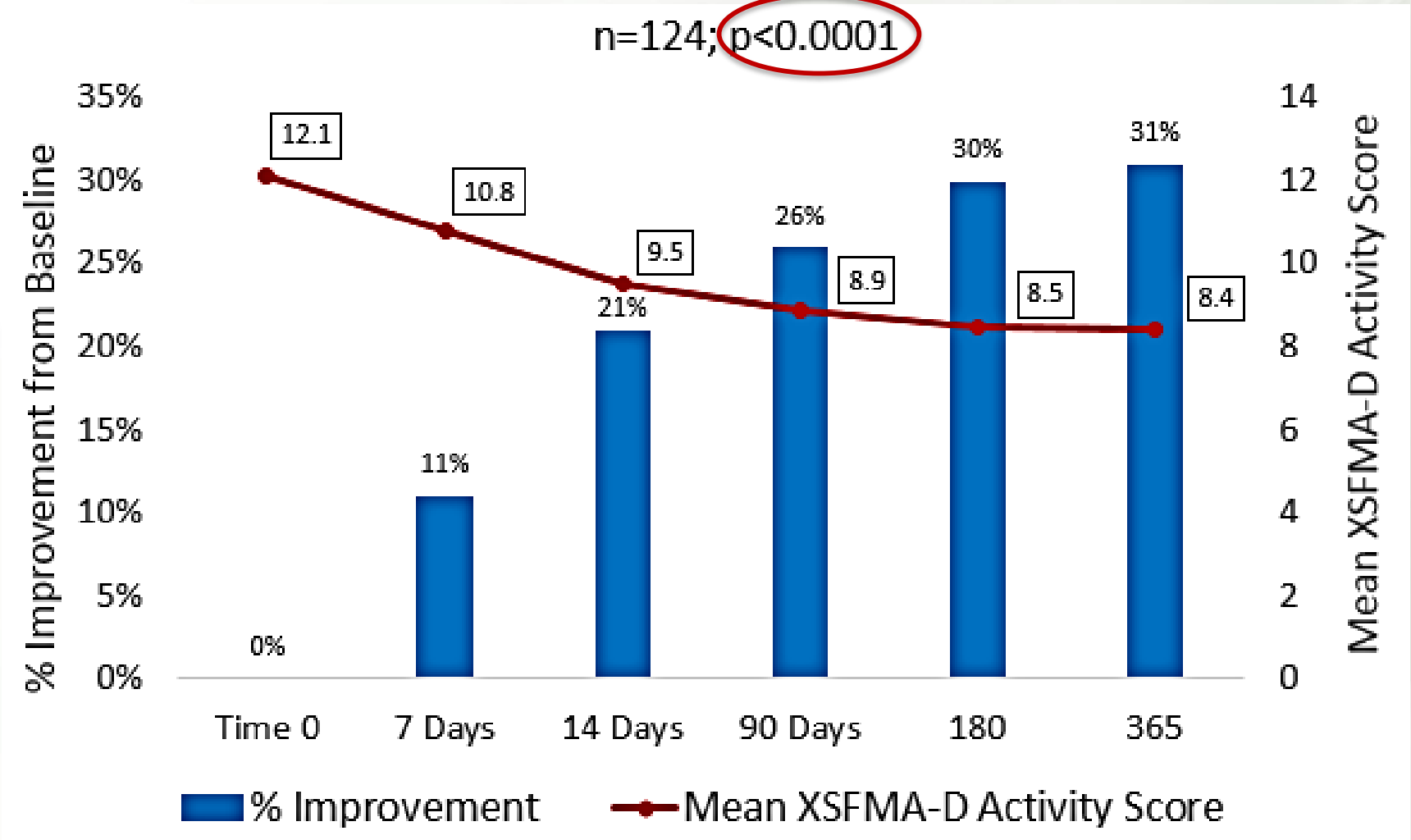
# Efficacy of Arthrokinex™ to Treat Knee OA

## Improved Knee Function



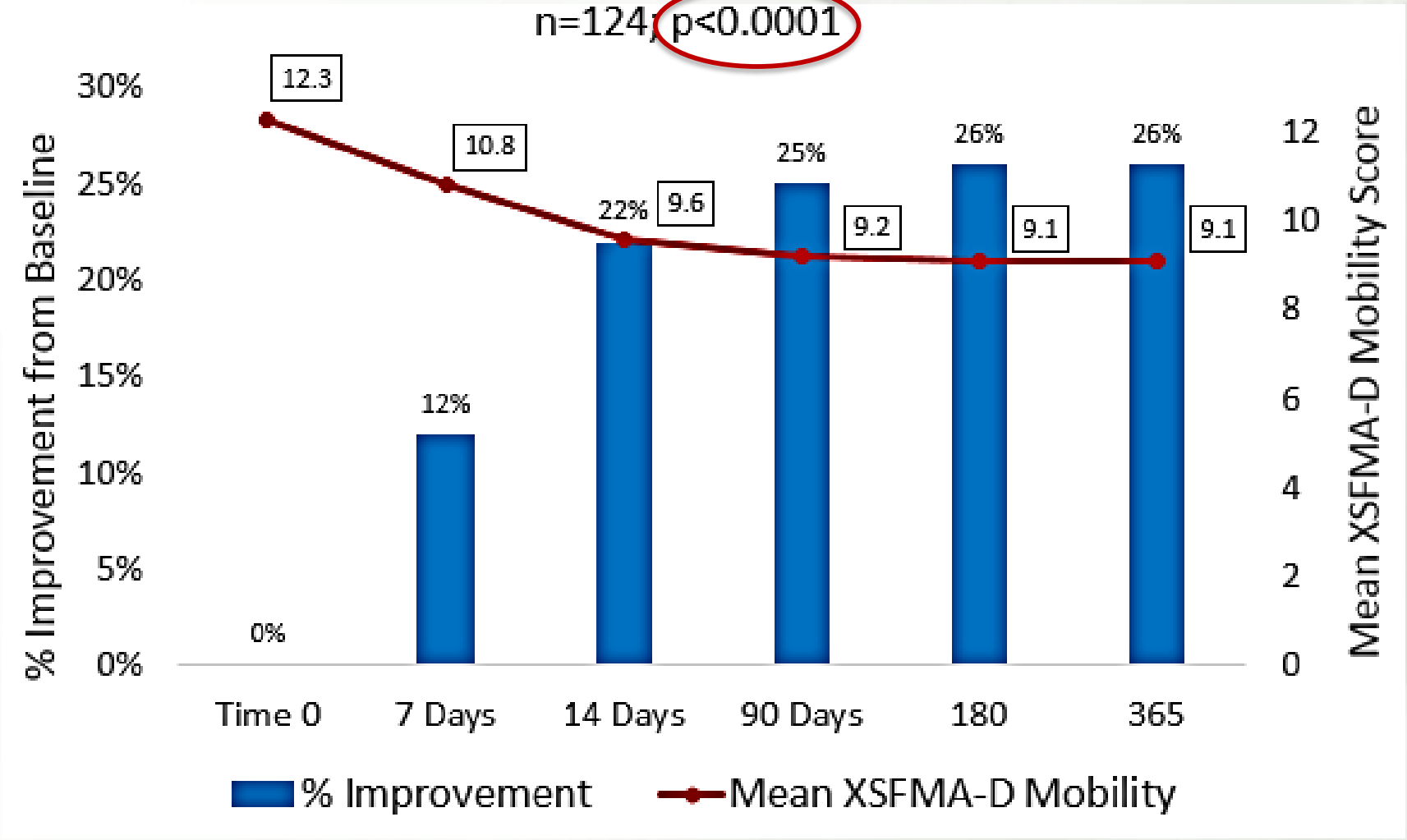
# Efficacy of Arthrokinex™ to Treat Knee OA

## Improved Knee Activity



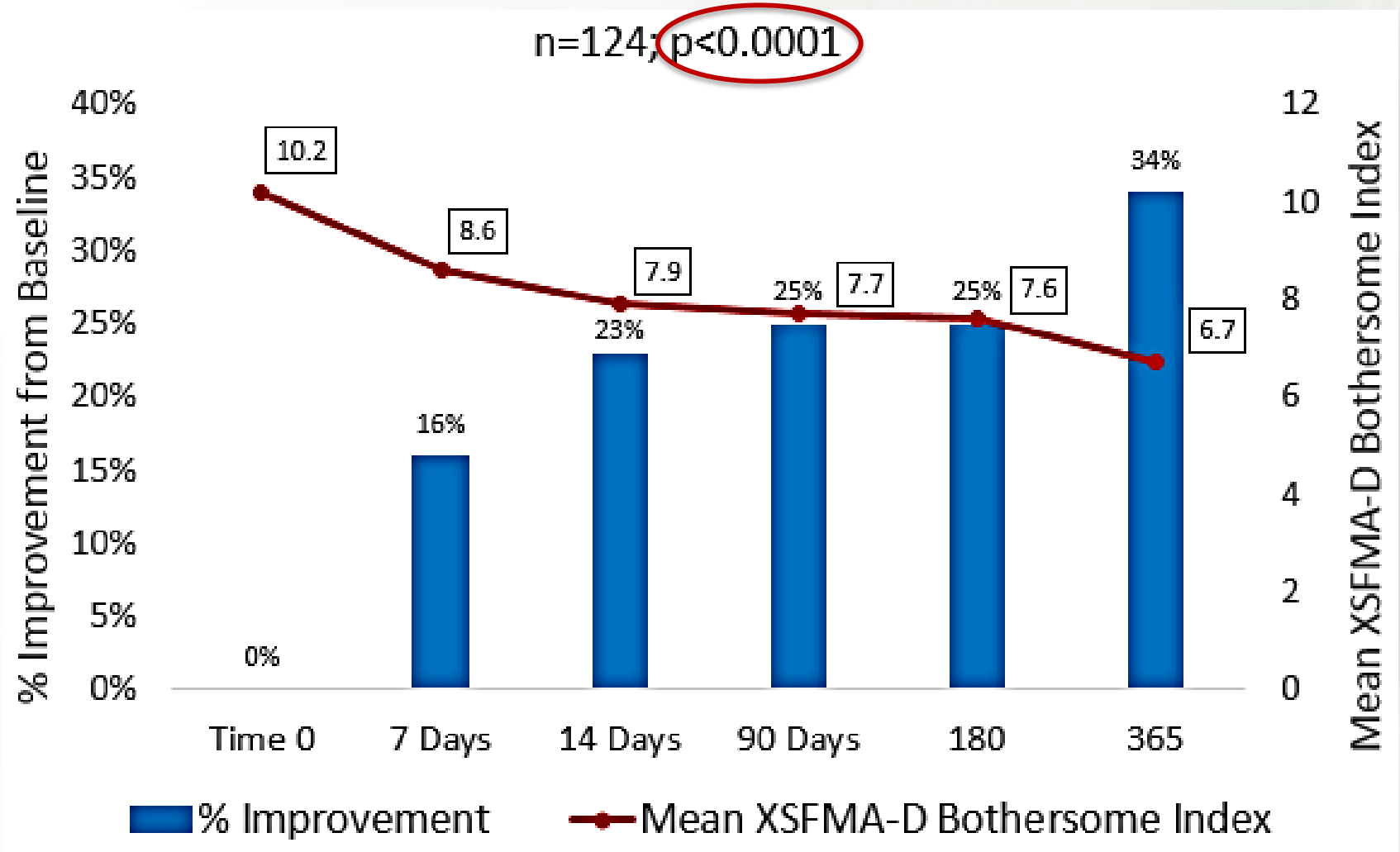
# Efficacy of Arthrokinex™ to Treat Knee OA

## Improved Knee Mobility

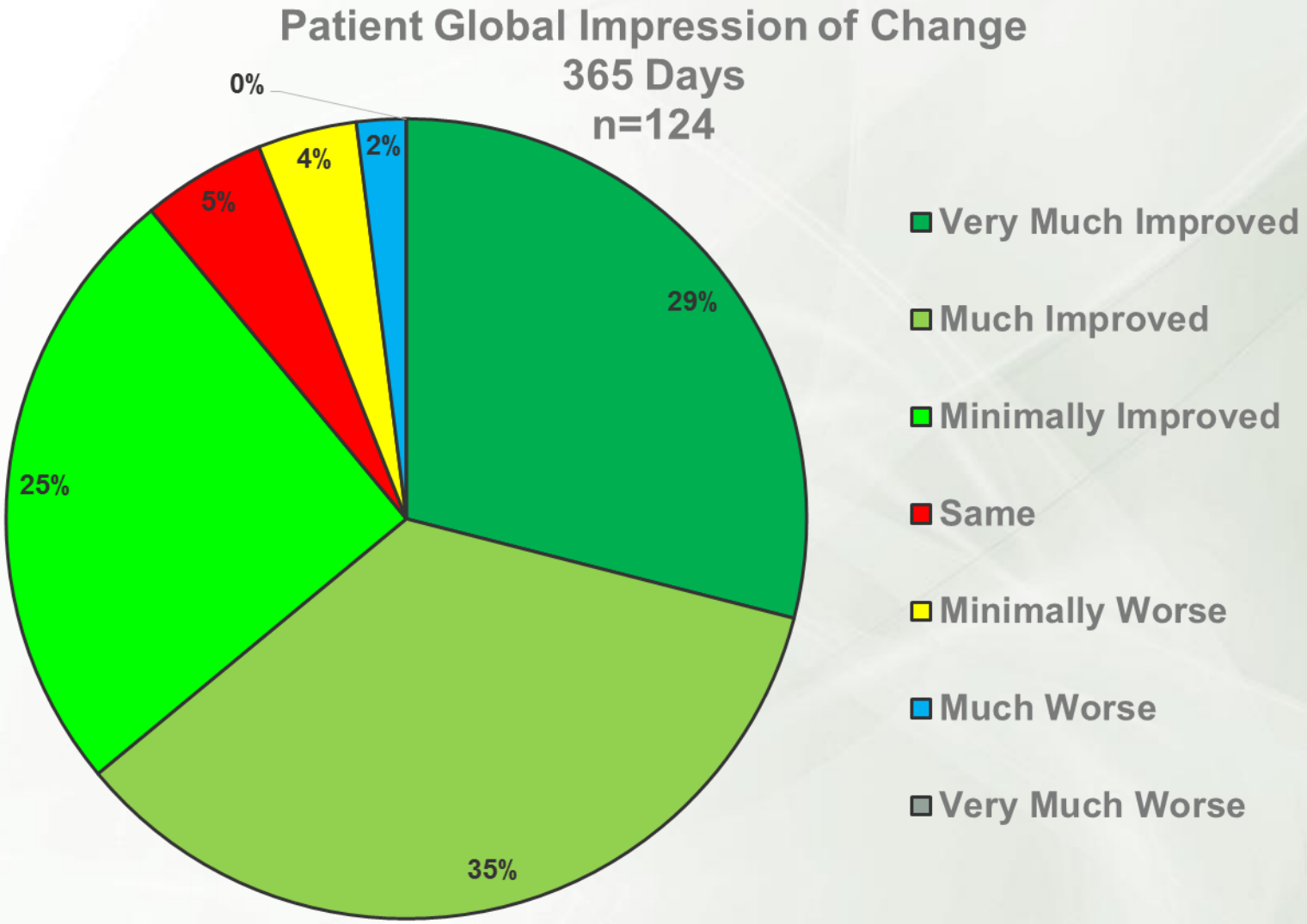


# Efficacy of Arthrokinex™ to Treat Knee OA

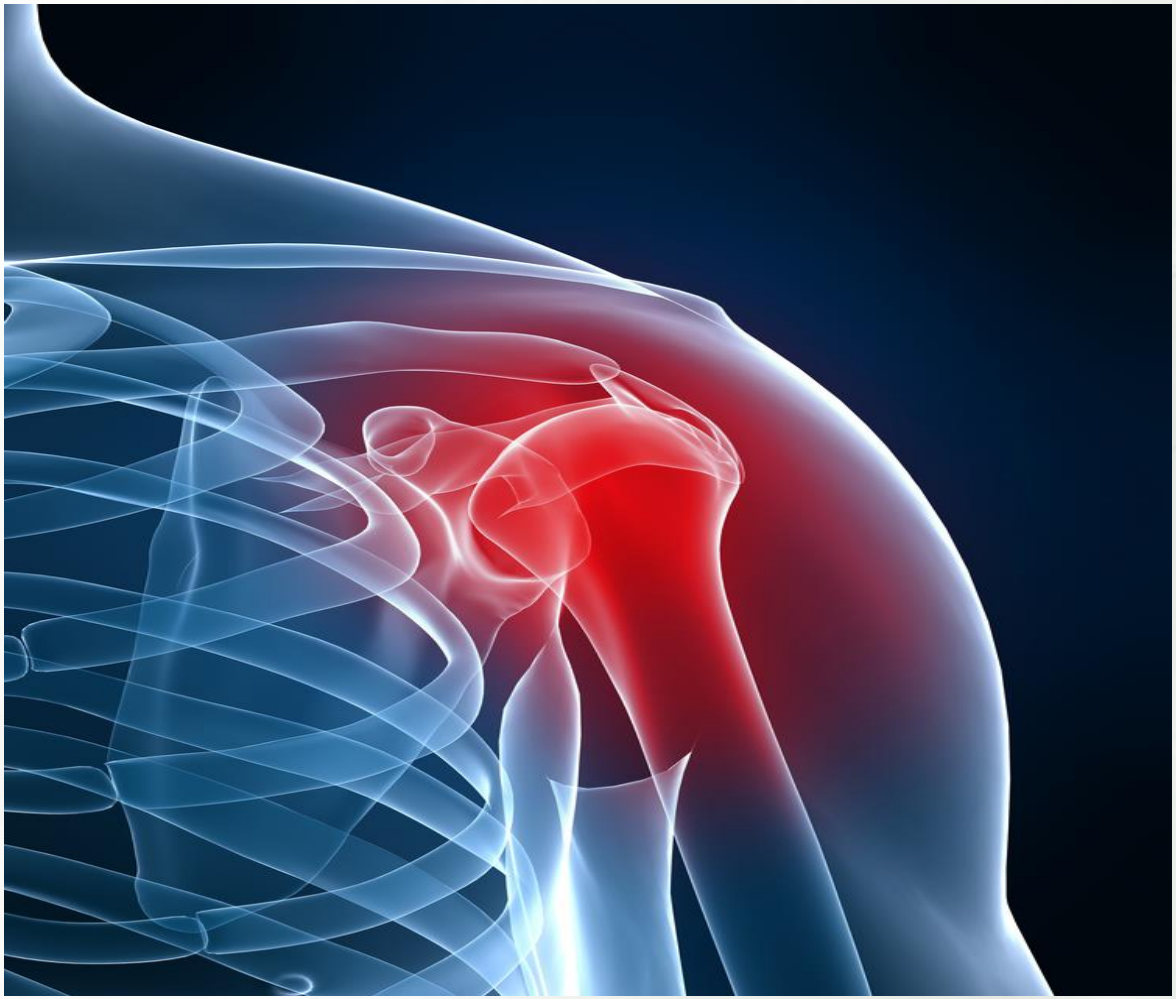
## Less Bothersome



# Efficacy of Arthrokinex™ to Treat Knee OA

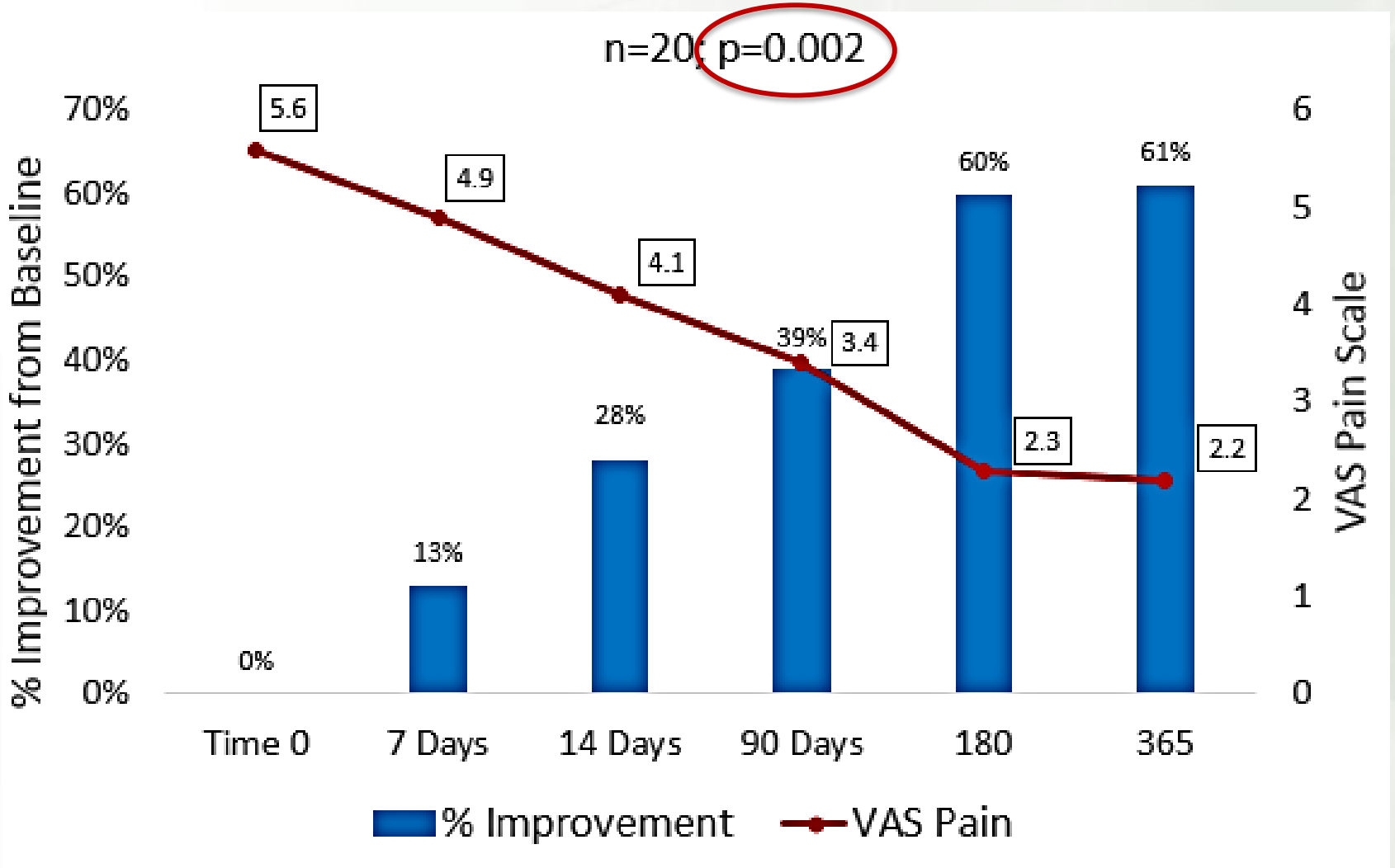


# The Shoulder



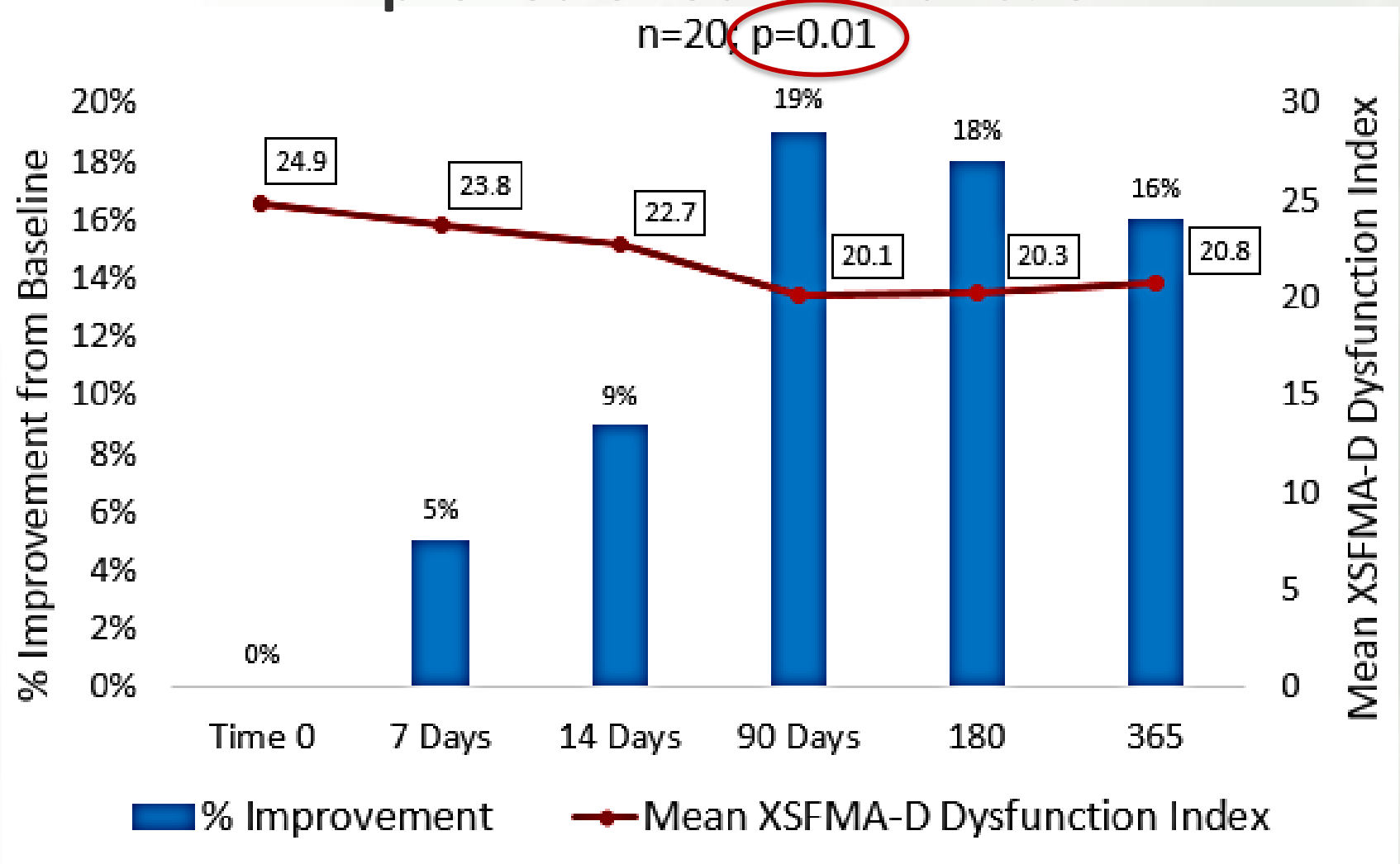
# Efficacy of Arthrokinex™ to Treat Shoulder OA

## Reduced Shoulder Pain



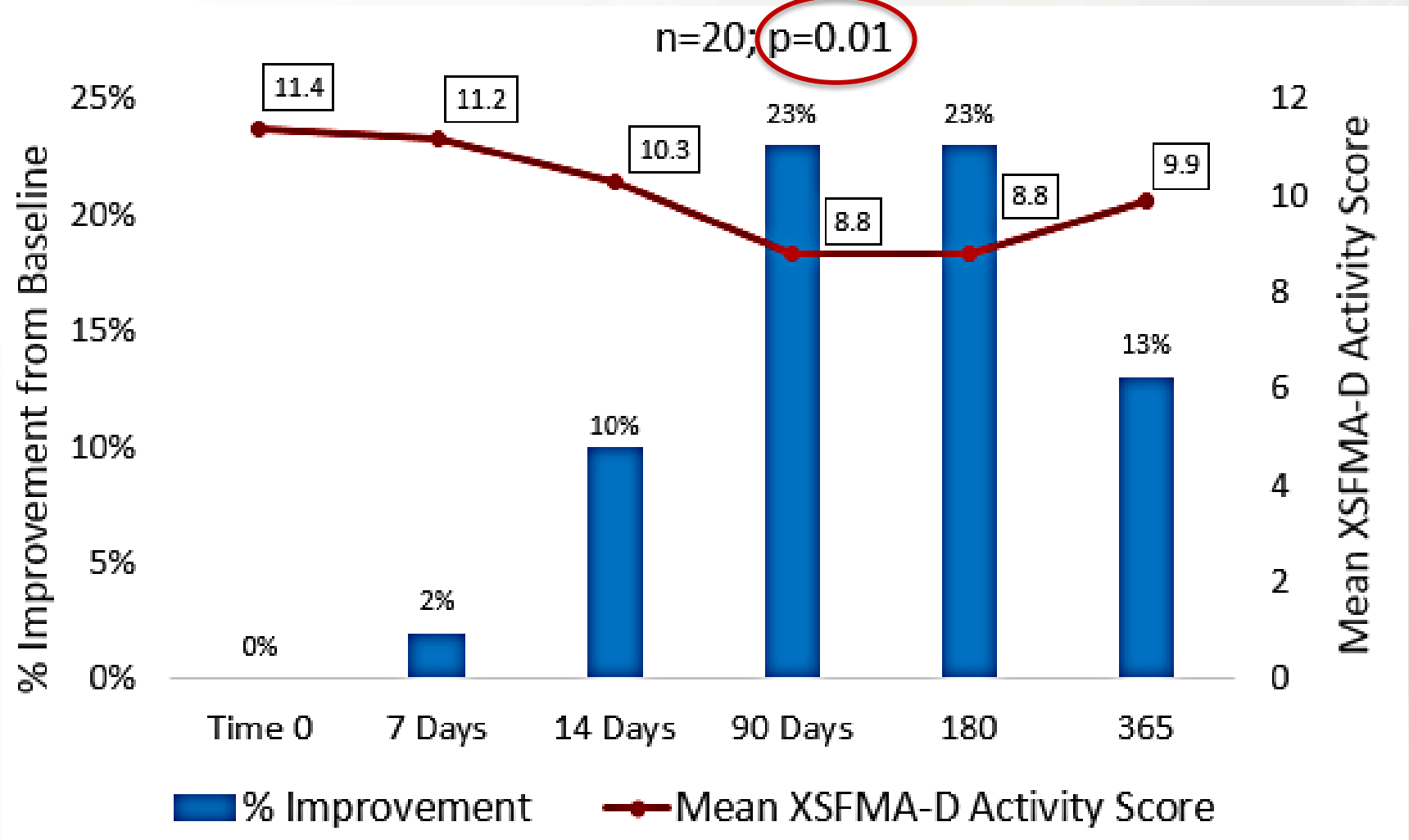
# Efficacy of Arthrokinex™ to Treat Shoulder OA

## Improved Shoulder Function



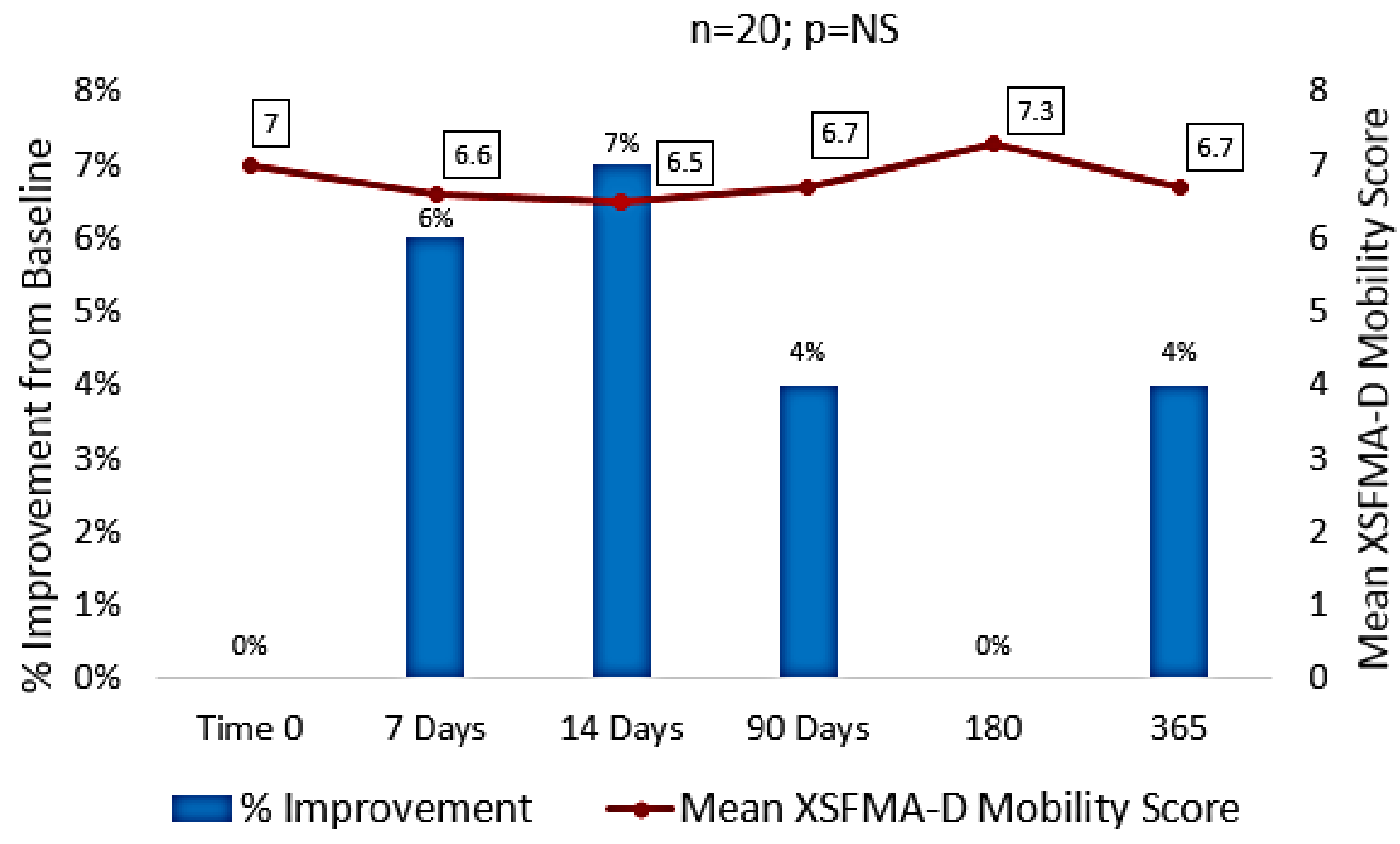
# Efficacy of Arthrokinex™ to Treat Shoulder OA

## Improved Shoulder Activity



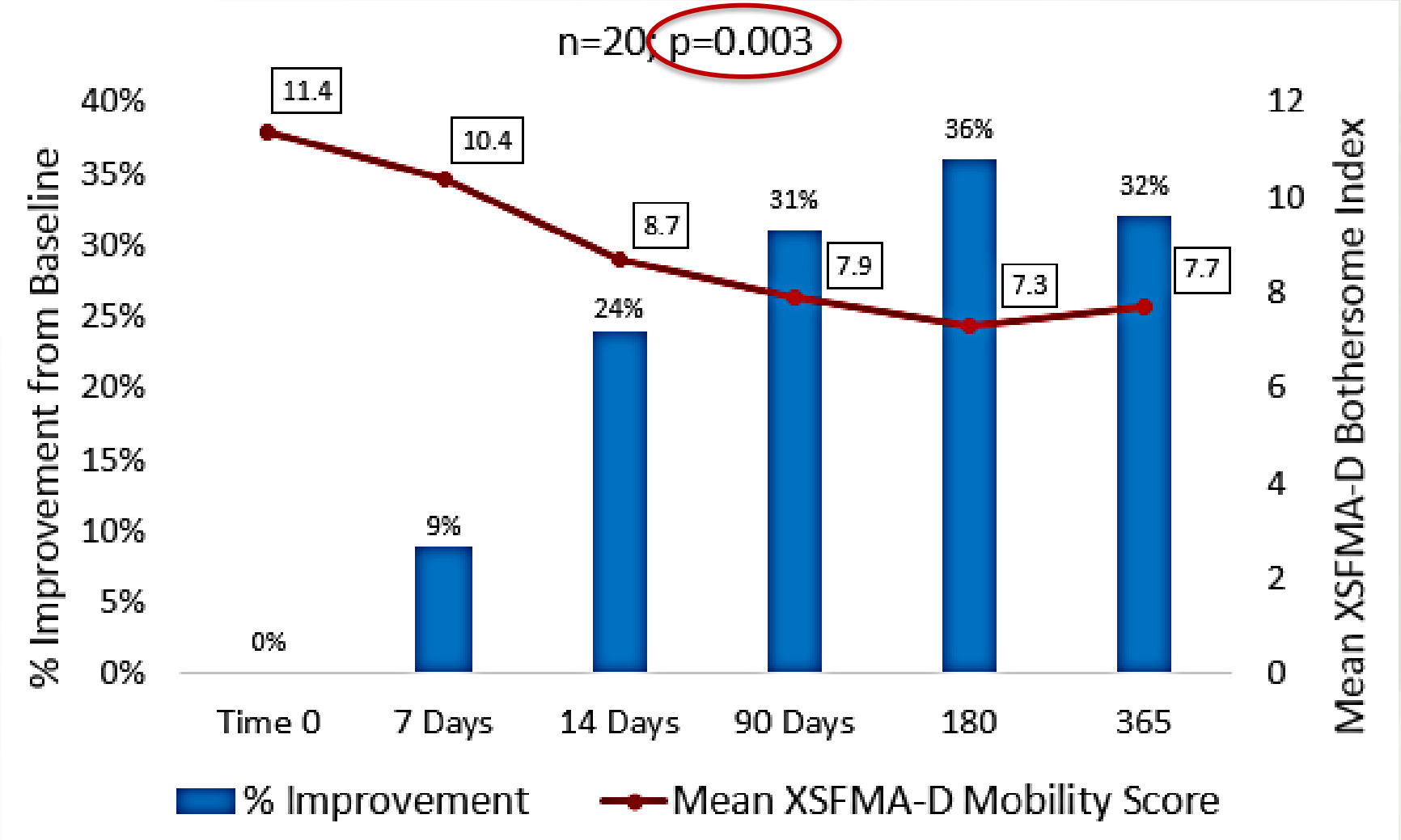
# Efficacy of Arthrokinex™ to Treat Shoulder OA

## Improved Shoulder Mobility

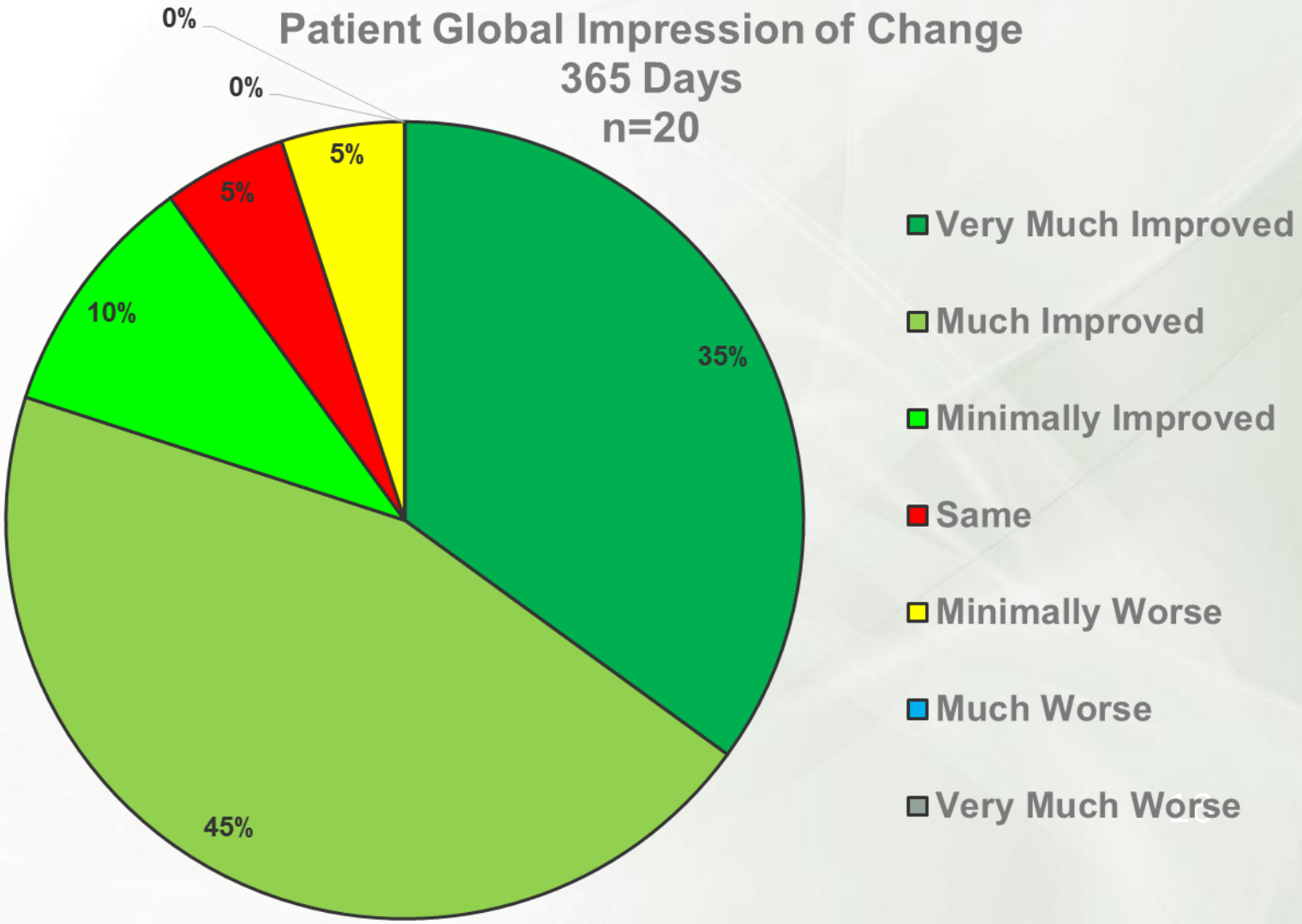


# Efficacy of Arthrokinex™ to Treat Shoulder OA

## Less Bothersome

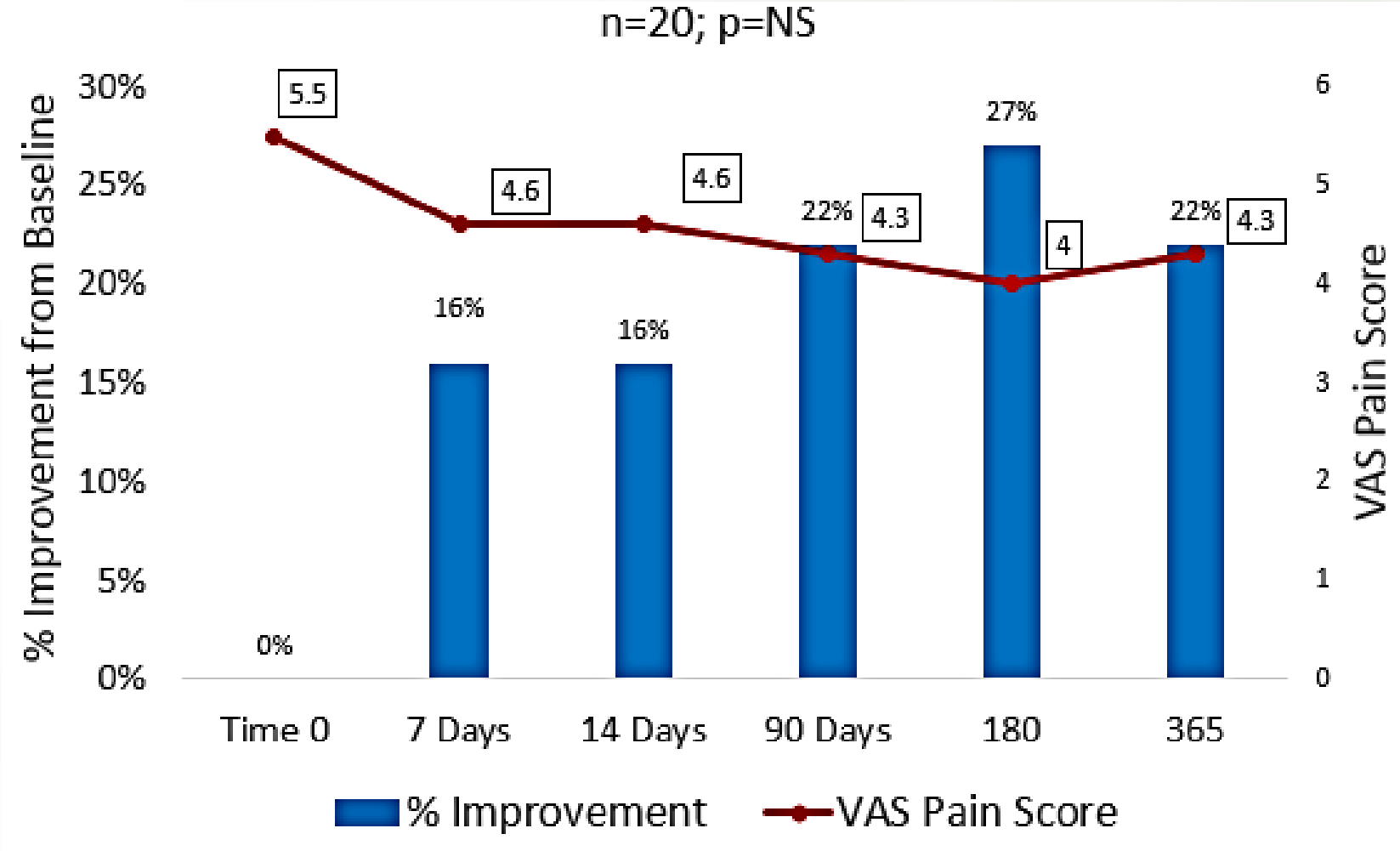


# Efficacy of Arthrokinex™ to Treat Shoulder OA

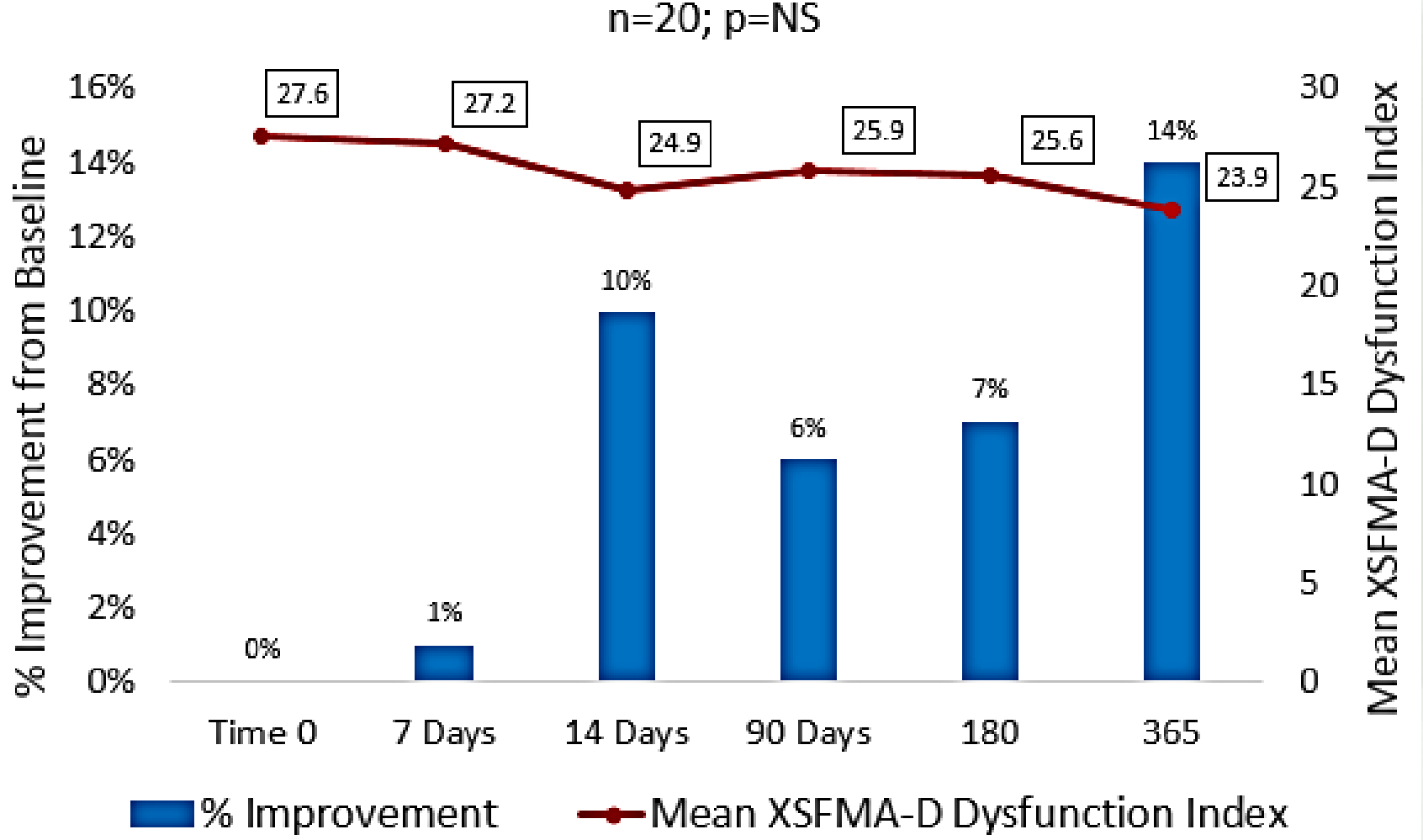


# The Hip

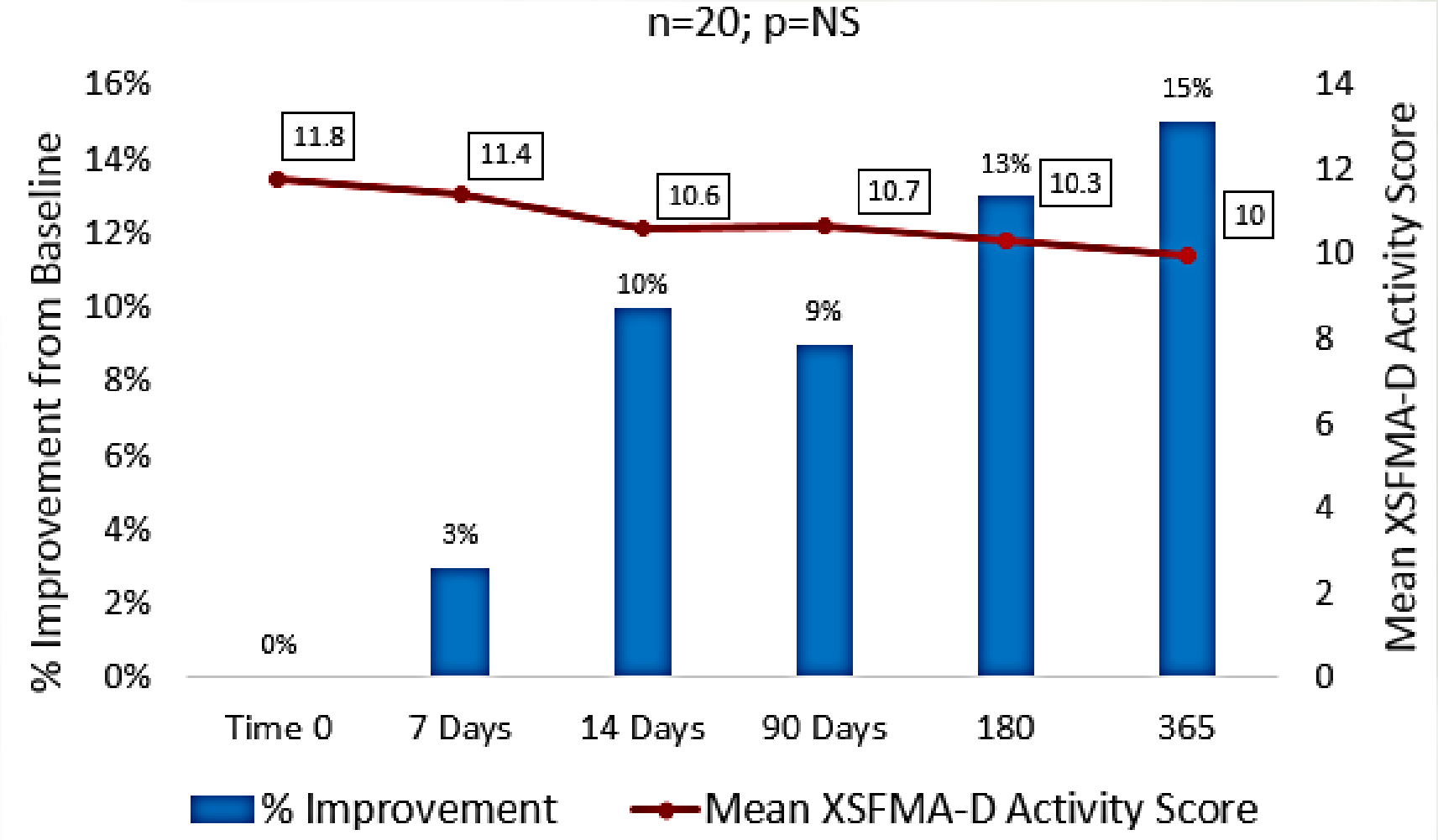
# Efficacy of Arthrokinex™ to Treat Hip OA
## **Reduced Hip Pain**



# Efficacy of Arthrokinex™ to Treat Hip OA
## Improved Hip Function

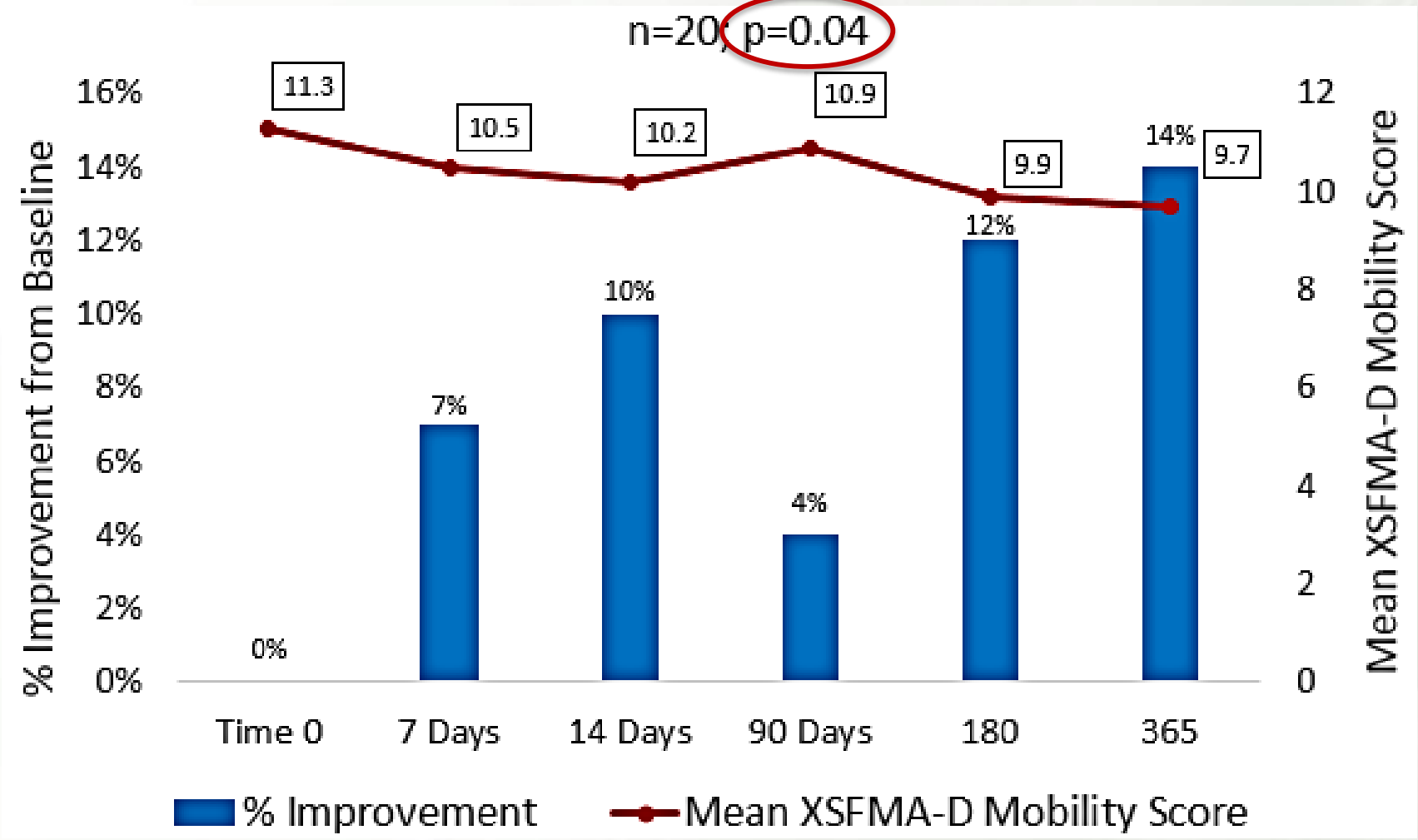


# Efficacy of Arthrokinex™ to Treat Hip OA
## Improved Hip Activity

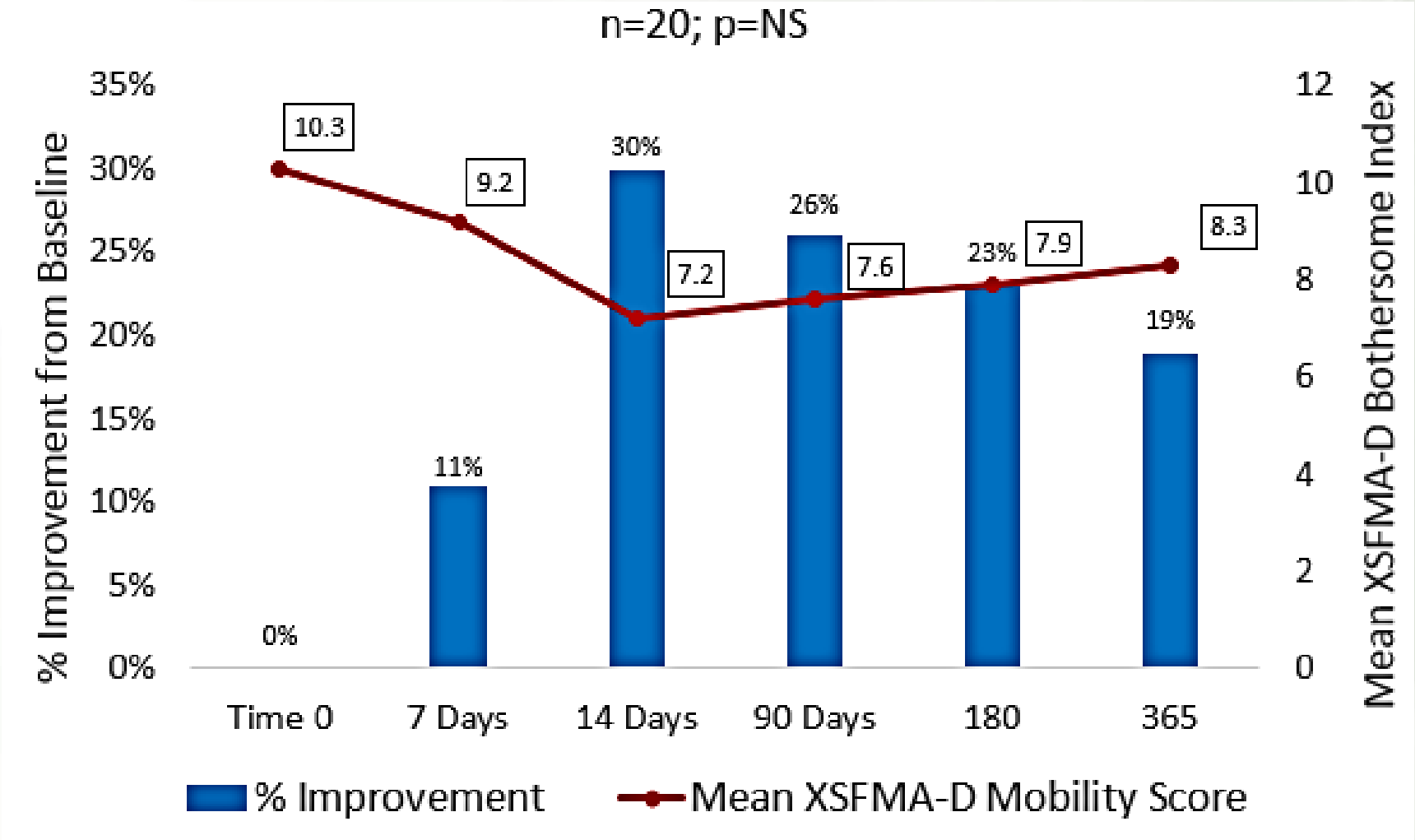


# Efficacy of Arthrokinex™ to Treat Hip OA

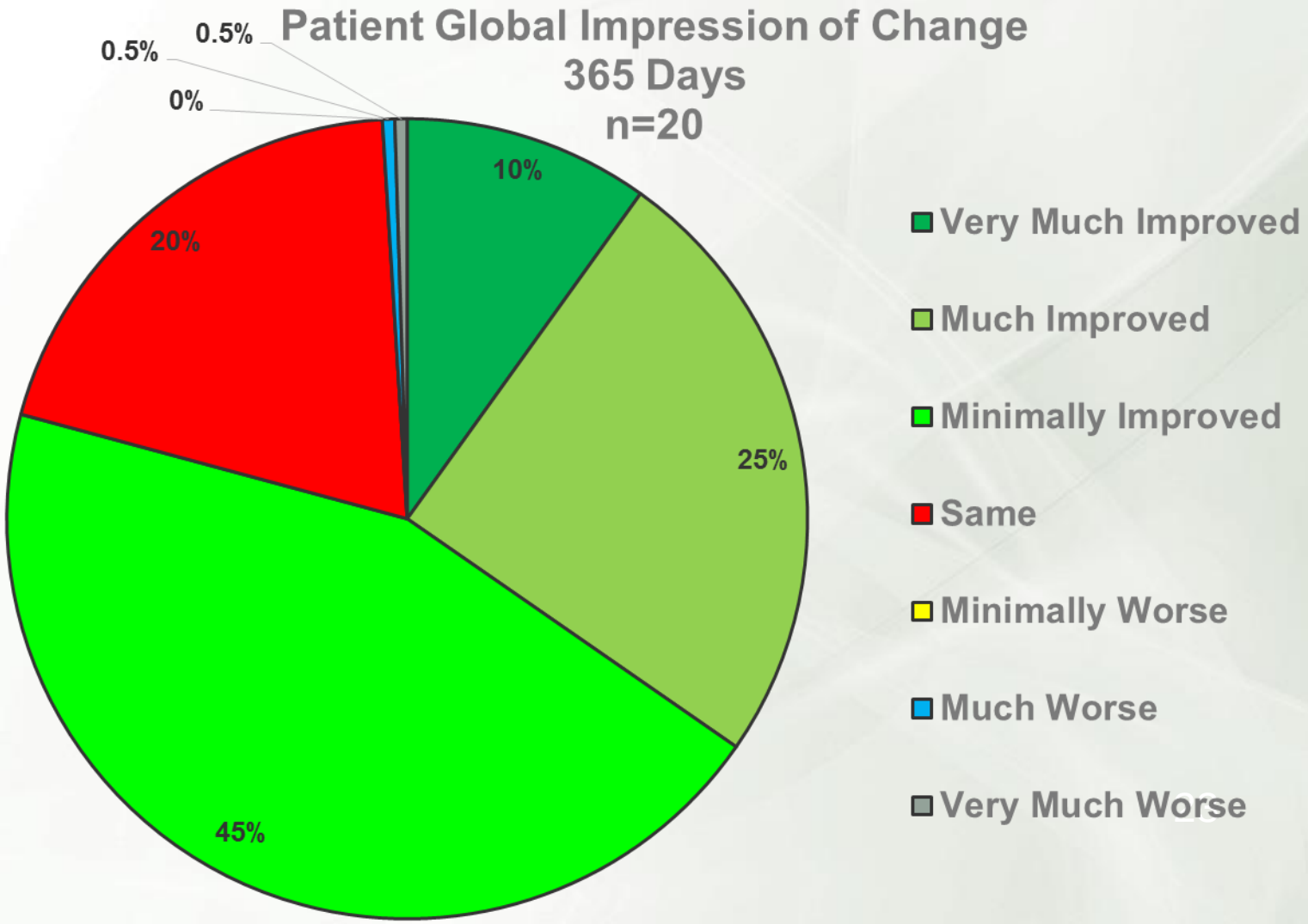
## Improved Hip Mobility



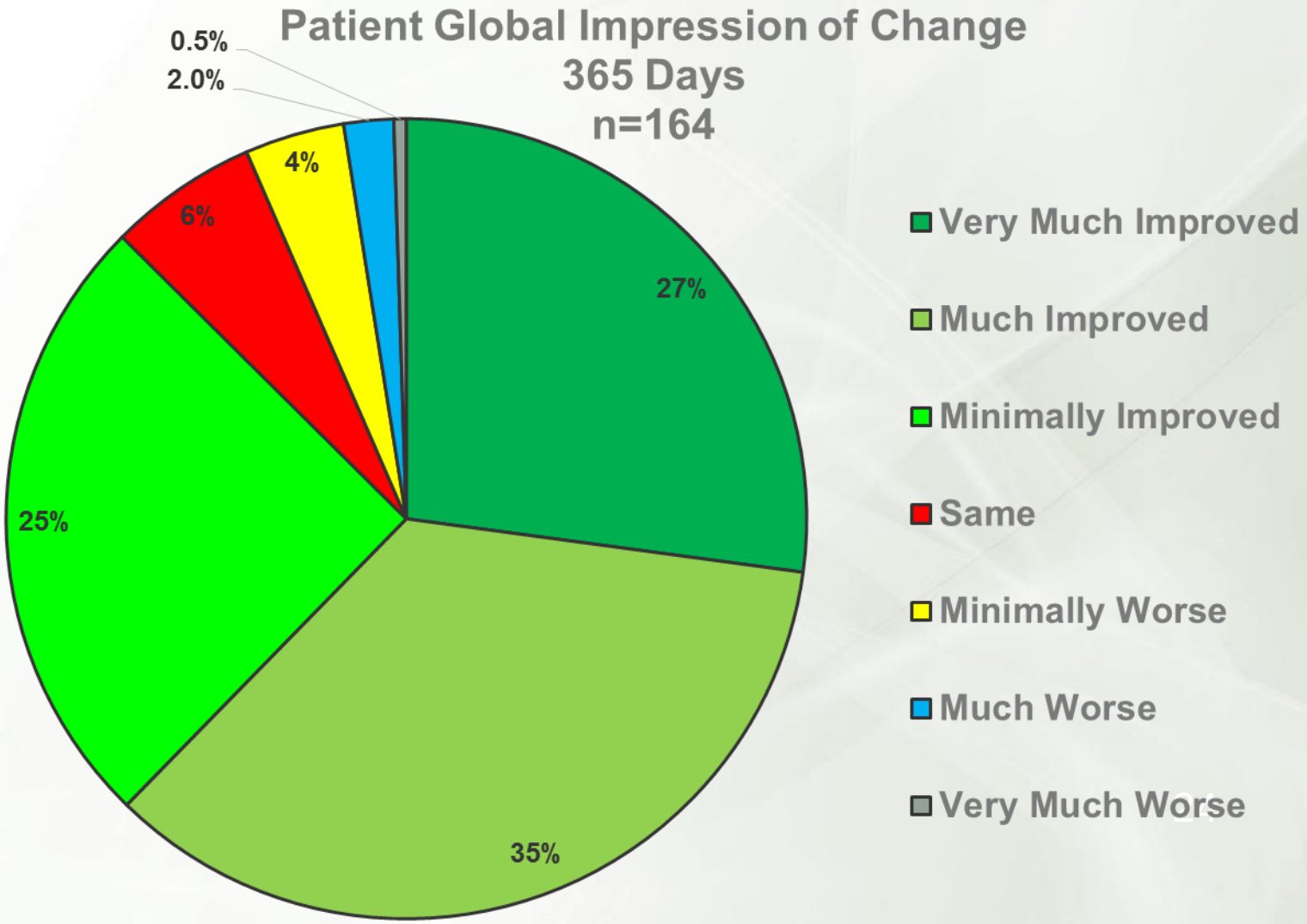
# Efficacy of Arthrokinex™ to Treat Hip OA
## Less Bothersome



# Efficacy of Arthrokinex™ to Treat Hip OA



# Knee, Shoulders and Hips Combined



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# A method to induce Interleukin-1 Receptor Antagonist Protein from autologous whole blood

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ABSTRACT

*Objective:* Current orthopedic therapies, aimed solely at symptomatic control, are unable to restore the cytokine imbalance that produces the hallmark clinical profile of osteoarthritis. While a myriad of chemical factors in the cytokine network stimulate local joint inflammation and pain, Interleukin 1 (IL-1) is widely recognized as a key offender and a potential therapeutic target. The purpose of this article is to describe a novel, on-site, point of service process (Arthrokinex™) to induce Interleukin 1 Receptor Antagonist Protein (IL-1-Ra or IRAP) from whole blood aimed at inhibiting the destructive intra-articular effects of IL-1.

*Methods:* 53 patient charts were included in this retrospective chart review study. Venous blood from the selected participants had been harvested and centrifuged to isolate Platelet Rich Plasma and Platelet Poor Plasma. These layers were extracted and incubated for 30 min in a specialized syringe containing medical grade concentrator beads. After centrifuge filtration, the supernatant containing IL-1-Ra was extracted. Anti-inflammatory (IL-1-Ra, IL-10) and pro-inflammatory (TNF α, IL-1 β) cytokines of baseline whole blood were compared to the conditioned serum following quantification using ELISA.

*Results:* On average, a 32-fold increase (baseline, 550 pg/mL; post conditioning 17,537 pg/mL) in IL-1-Ra concentration was observed after the brief interaction of blood with the concentrator bead surface. IL-1-Ra, if present in concentrations that are 10–100 times higher than IL-1β, will block the interaction of IL-1β with cell surface receptors. At these increased concentrations, Arthrokinex™ induced IL-1-Ra joint injections produce an IL-1-Ra to IL-1β ratio of 999:1. Post conditioning levels of IL-1β and TNF α were not clinically significant.

*Conclusion:* The Arthrokinex™ blood conditioning process has the ability to rapidly induce IL-1-Ra without increasing the pro-inflammatory cytokine profile.



## 1. Introduction

The poorly understood, multi-factorial pathogenesis of osteoarthritis (OA) provides a significant challenge to treat the estimated 27 million people in the US [1] affected by the progressively debilitating disease. Articular cartilage destruction, subchondral bone remodeling and synovitis are the chief causes of the clinical manifestation of OA, which include pain, swelling, and stiffness of the affected joint. Axiomatically, these symptoms can pose a dramatic hindrance on daily activities depending on severity. Analgesic drugs, nonsteroidal anti-inflammatory drugs (NSAIDs) and intra-articular (IA) corticosteroid injections are the currently recommended pharmacologic interventions for knee OA [2]. Given the limited scope and effectiveness of these treatment options aimed solely at symptomatic control of the disease, many patients are forced to undergo surgery. Regenerative therapies including platelet rich plasma and mesenchymal stem cells, are on the rise despite conflicting evidence of supportive data. Early data indicated the potential musculoskeletal benefits and cost effectiveness of platelet rich plasma (PRP) injections. The majority of trials have failed to provide evidence for the increased use of PRP therapy [3]; however it is difficult to pinpoint if this is due to the actual treatment regimen or the lack of standardized protocols, platelet separation techniques and outcome measures. Interestingly, a recent systemic review and meta-analysis reported PRP IA injections are significantly superior to placebo and hyaluronic acid for the treatment of knee OA (all other outcomes were excluded) [4]. Despite inconsistent results, the market value of

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1043-4666/

PRP is estimated to reach $126 million by 2016 [5]. A number of recent studies are beginning to emerge that reveal the potential for autologous adipose tissue derived mesenchymal stem cells, albeit to a much smaller degree than PRP, for the treatment of OA [6]. The need for an out-patient, on-site, point of service, low cost symptom relieving and possibly chondroprotective drug is evident given the already high prevalence of arthritis in the US, which is expected to increase to nearly 67 million people by the year 2030 [7], the significant financial burden to the patient ($703/year) and insurer ($3080/year) [8] and the lack of effective non-surgical options.

A recently improved knowledge of the molecular mechanisms underlying this disease has led to the exploration of biotherapeutic strategies. One approach that holds promise is the inhibition of interleukin-1β (IL-1 β), a major cytokine promoting the catabolic activity associated with OA affected joints [9]. Attur et al. [10] reported the presence of biologically active IL-1β in OA-damaged cartilage providing the rationale to explore blockade of this molecule as a target to facilitate cartilage repair and potentially reverse degradation. Different methods to specifically inhibit Interleukin 1 (IL-1) have been tested. Briefly, those include the application of soluble IL-1 receptors, monoclonal antibodies against IL-1 or IL-1 receptor 1, blocking the formation of active IL-1β, gene therapy, and the application of IL-1 receptor antagonist protein (IL-1-Ra) [9], which serves as the focus of this investigation. It is unclear which method is most effective; however, the success of three commercially available IL-1-Ra products (recombinant Anakinra™, autologous Orthokine™ and Arthrex™) led to the development of our novel IL-1-Ra formulation process. The primary purpose of this investigation was to test our hypothesis that our on-site, point of service, minimal manipulation processing of whole blood would induce sufficient IL-1-Ra levels and IL-1-Ra:IL-1β block ratios. Secondary outcomes were twofold: (1) to ensure the Arthrokinex™ process did not increase the concentration of anti-inflammatory cytokines (TNF-α and IL-1β) and (2) to evaluate cytokines levels in the serum samples after being stored at −20 °C for at least one year.

## 2. Materials and methods

### 2.1. Study design

This was a retrospective chart review/proof of concept investigation aimed to quantify the ability of the Arthrokinex™ process to enhance IL-1-Ra in whole blood. All aspects of the study protocol were extensively reviewed and approved by IntegReview Institutional Review Board (IRB) as being considered exempt from requiring IRB approval as it met all requirements outlined in 45 CFR 46.101(b)(4), specifically (1) the research involves only the collection or study of pre-existing data, documents, records, pathologic specimens or diagnostic specimens and (2) the information will be recorded in such a manner that the subjects cannot be identified, directly or through identifiers linked to the subjects.

### 2.2. Participants

Existing charts were reviewed and a total of fifty three (53) patient charts met all inclusion criteria for this analysis: age >21 years, chronic OA for at least 3 months, patients were diagnosed with OA according to the American College of Rheumatology (ACR) criteria, radiographic evidence of OA and ⩾4 pain grade (on a numeric scale of 1–10). Exclusion criteria included: patient charts of those in generally poor health, pregnant or breast feeding, drug dependent (chronic opioid use, alcohol, etc.), undergone surgery or treatment of the affected joint within the last 3 months, lacked the mental ability to understand the treatment plan, systemic disease of the musculoskeletal system, bone cancer, metastasis or tumor-like lesions in the immediate proximity to the treated joint, fracture in the last 3 months, acute bacterial infection, blood clotting disorders, major psychiatric disease requiring therapy, and continuous corticoid or NSAID therapy due to other diseases. Informed consent was obtained from each participant and all work was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

### 2.3. Processing of whole blood (Arthrokinex™)

Using aseptic techniques, 60 mL whole blood from the median cubital vein of fifty three (53) participants was harvested into a sterile 60 mL syringe containing 3 mL of anticoagulant citrate dextrose (ACD) solution and centrifuged (3200 rpm, 15 min). The resultant Platelet Rich Plasma (PRP) and Platelet Poor Plasma (PPP) were then extracted and the remaining layers, containing buffy coat and erythrocytes, were discarded. Both the PRP and PPP were transferred to a specialized, closed-system, centrifuge tube containing medical grade concentrator beads, mixed and allowed to incubate for 30 min at ambient temperature. After the short incubation period, centrifuge filtration (2000 rpm, 3 1/2 min) through a sterile 0.45 μm filter was completed and the resulting sterile filtrate was slowly drawn into 1 mL syringes. The 1 mL syringes could be used immediately for intra-articular injection or stored at −20 °C for future use.

### 2.4. Biomarker assays

The primary outcome of measuring IL-1-Ra (pre- and post-conditioning) was achieved by using the highly sensitive, commercially available quantitative sandwich enzyme-linked immunoassay technique (R&D Systems, Quantikine ELISA; Minneapolis, MN, USA. The manufacturer reports this kit, when run in accordance with standard Quantikine protocols, to be extremely sensitive (minimum detectable dose ranged from 2.2 to 18.3 pg/mL), specific (no significant cross-reactivity or interference was observed), precise (intra- and inter-assay CVs were 3.7% and 6.7%) and linear (all diluted samples fell with the dynamic range of the assay). Since sample concentrations were expected to fall outside the range of provided standards, serum was diluted 100 fold by adding 5 μl of sample to 495 μl of calibrator diluent. Resulting concentrations were calculated by subtracting the average zero standard optical density and log transforming IL-1-Ra concentrations versus the log of the optic density on a linear scale, and the best fit line determined by regression analysis. IL-1-Ra concentrations were only accepted if the standard curve correlation coefficient (r) reached 0.99 and the CV of each sample was under 20%.

As a secondary outcome, serum levels (pre- and post-conditioning) of pro-inflammatory (TNFα, IL-1β) cytokines and another anti-inflammatory cytokine (IL-10) were measured separately using ELISA. All kits reported comparable sensitivity, specificity, precision and linearity as described above. Similar to IL-1-Ra, all kits were run in accordance with standard Quantikine protocols.

### 2.5. Statistical analysis

SPSS 12.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Wilcoxon signed rank test were performed to analyze the statistical difference between baseline and post-processing cytokine levels. All results shown are the mean ± SEM of two or more experiments.

## 3. Results

### 3.1. Participant characteristics

Of the 53 participants, 25 men and 28 women were included. The mean age was 59.8, ranging from 25 to 85 years. According to the World Health Organization guidelines, 16 of the 53 (30%) participants were classified as overweight (BMI ⩾ 25 kg/m$^2$) and 30 participants (57%) are classified as obese (BMI ⩾ 30 kg/m$^2$). Of the 30 obese patients, 21 fall into the category of class I obesity (BMI 30–34.99 kg/m$^2$), 6 were classified as class II obese (BMI 35–39.99 kg/m$^2$) and 3 were characterized as class III obese (BMI ⩾ 40 kg/m$^2$) (Table 1).

### 3.2. Primary outcome: Arthrokinex™ process induced IL-1-Ra levels

Autologous conditioned serum resulted in a markedly increased induction of Arthrokinex™-derived IL-1-Ra (17,537 ± 1234 pg/mL) (Table 2). These values are comparable to IL-1-Ra levels produced by Orthokine™ [11] and Arthrex™ [12]. On average, after the short 30 min incubation period, a 32 fold increase in IL-1-Ra was observed between baseline and post-Artrhokinex™ serum. IL-1-Ra levels increased by at least a factor of 10 in 50 (out of 53) serum samples. Furthermore, 5 samples obtained IL-1-Ra levels that increased at least 20 times from baseline, 14 samples that increased at least 30 times from baseline, 11 samples that increased at least 40 times from baseline and 13 samples that increased at least 50 times from baseline. One sample increased by a factor 120, representing the highest increase of IL-1-Ra observed. This robust and rapid increase in IL-1-Ra synthesis resulted in a mean serum IL-1-Ra to IL-1β ratio of 999.0 (Fig. 1).

### 3.3. Secondary outcomes: IL-10, TNF-α, IL-1β

In addition to the 32 fold increase in IL-1-Ra, a statistically significant increase in the anti-inflammatory Interleukin 10 cytokine ($p < 0.001$) was observed. Despite this statistical significance, the clinical significance of this increase is negligible. A statistical increase was also observed in the pre and post-Arthrokinex™ levels of IL-1β and TNF α (Table 2); however, similar to IL-10, these increases are not clinically significant.

### 3.4. Storage of autologous conditioned serum

Following our novel conditioning process, approximately 6–12 mL of concentrated IL-1-Ra rich serum is extracted. In order to test the storage capacity of Arthrokinex™, a small, separate subset of patients' (n = 21) conditioned sera that had been stored at −20 °C for at least one year was analyzed using ELISA. Mean IL-1-Ra levels remained markedly elevated (16,167 ± 109 pg/mL) and were similar to mean levels of IL-1-Ra observed soon after processing. A similar trend was observed in each of the additional cytokine levels measured in this investigation (IL-10, 31.9 ± 4.1 pg/mL; IL-1β, 42.5 ± 3.7 pg/mL, TNFα, 13.1 ± 0.7 pg/mL).

**Table 1**
Patient demographics and clinical characteristics.

| | |
|---|---|
| N | 53 |
| Male/female | 25/28 |
| Mean age (range) | 59.8 (25–85) |
| BMI classification | |
| Overweight (BMI ⩾ 25 kg/m$^2$) | 16/53 (30%) |
| Obese Class I (BMI 30–34.99 kg/m$^2$) | 21/53 (40%) |
| Obese Class II (BMI 35–39.99 kg/m$^2$) | 6/53 (11%) |
| Obese Class III (BMI ⩾ 40 kg/m$^2$) | 3/53 (6%) |

**Table 2**
Cytokine induction following Arthrokinex™ procedure.

| | Baseline (pg/mL) | Post-Arthrokinex™ (pg/mL) | Fold increase | P value |
|---|---|---|---|---|
| IL-1-Ra | 549.6 ± 52.6 | 17,537 ± 1234 | 31.9 | <0.0001 |
| IL-1 β | 7.3 ± 0.8 | 17.5 ± 2.0 | 2.4 | <0.0001 |
| IL-10 | 24.9 ± 2.7 | 31.7 ± 4.8 | 1.3 | <0.001 |
| TNFα | 9.8 ± 1.9 | 24.9 ± 2.7 | 2.5 | <0.0001 |

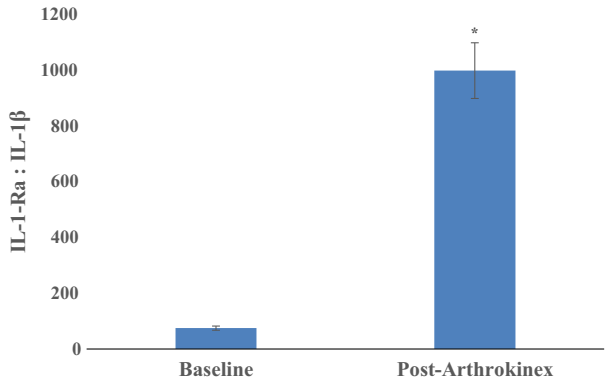


**Fig. 1.** Autologous conditioned serum (Arthrokinex™) produces a favorable cytokine profile by shifting the anti-inflammatory to pro-inflammatory ratio. Enhanced concentration of IL-1-Ra has the potential to block the destructive effects of IL-1β.

## 4. Discussion

The primary aim of this investigation was to determine the capacity of the Arthrokinex™ conditioning process to induce synthesis of IL-1-Ra from a patient's whole blood. The desired therapeutic effect of Arthrokinex™ is facilitated by the ability of IL-1-Ra to limit the destructive inflammatory intra-articular actions of IL-1β. Supranormal levels of IL-1β and TNFα, mainly produced by activated synoviocytes, mononuclear cells and articular cartilage, drive the catabolic response and augment the pathogenesis of OA by stimulating release of other cytokines (IL-8, IL-6 and nitric oxide) and prostaglandin $E_2$. Additionally, IL-1β and TNFα can increase their own production through autocrine signaling which could further shift the equilibrium between IL-1β and IL-1-Ra. All of these cytokines diffuse into the synovial fluid and promote cartilage matrix degradation [13].

Consistent with previous studies designed to physico-chemically induce anti-inflammatory cytokines [11,14,15], our novel process provides sufficient levels of IL-1-Ra to competitively inhibit IL-1β [15]. IL-1-Ra, if present in concentrations that are 10–100 times higher than IL-1β, will block the interaction of IL-1β with cell surface receptors as well as soluble IL-1R type 2 [16]. The volume of the synovial fluid in an OA-affected knee increases to approximately 13.6 mL [17] and contains 34 pg (2.5 pg/mL) of IL-1β [18]. All serum levels in this trial exceeded the 100:1 threshold so it is therefore reasonable to conclude that Arthrokinex™ can consistently produce IL-1-Ra levels that will inhibit IL-1β.

The capability of IL-1-Ra to treat knee OA symptoms is confirmed in some [14,15], but not all [19] clinical trials. The largest trial (n = 376) conducted by Baltzer et al. [14], was designed to compare the clinical effectiveness of intra-articularly administered IL-1-Ra (Orthokine™) to hyaluronan (HA) and saline. Patients in each group had two appointments with a physician per week for three consecutive weeks. Patients in the saline and HA group received a total of three injections and the patients in the IL-1-Ra

group received a total of six injections. Orthokine™-treated patients showed significant improvements in all outcome measures compared to HA and saline-treated patients. Certainly, the slightly different treatment regimens among groups should be considered; however, this preliminary study provides evidence for the efficacy of intra-articular administration of IL-1-Ra as a treatment strategy to combat the immobilizing effects of knee OA. Previously, Yang et al. [15] reported a superior biological response elicited by Orthokine™ compared to physiological saline in the treatment of knee OA. Despite the comparable improvement on the WOMAC in patients treated with Orthokine™ and placebo, KOOS (Knee Injury and Osteoarthritis Outcome Score) symptoms and sport parameters were significantly improved in the treatment group. Additionally, other clinical observations in Orthokine™-treated patients were consistently improved but were not statistically significant. Ultimately, the authors concluded the use of Orthokine™ cannot yet be recommended for the treatment of knee OA since the primary outcome of the investigation, 30% improvement in WOMAC between groups, was not met.

Surprisingly, several recent review articles [20–22] have ignored the success of Orthokine™, but instead focused solely on the inability of Anakinra™ to provide symptomatic relief of KOA that was significantly superior to placebo. In an open label randomized, multicenter, double-blind, placebo-controlled trial (n = 160), patients were divided into 3 groups and received a single intra-articular dose of Anakinra™ (150 mg or 50 mg) or placebo [20]. After 4 weeks, WOMAC global scores for all group improved with a non-significant difference between placebo and Anakinra™ 50 mg and between placebo and Anakinra™ 150 mg. A statistically significant improvement ($p = 0.051$) was approached between the placebo group and the Anakinra™ 150 mg group in the WOMAC pain sub-score on day 4. However, it is difficult to directly compare this trial to previous findings since only a single injection was administered. Additional trials are needed to determine whether repeated injections deliver therapeutic levels of IL-1-Ra to reduce pain.

Several clinical human trials have reported improved clinical outcomes of patients with muscle [23] and ligament injury [24–28] as well as spinal disorders [29] following IL-1-Ra treatment. Of particular interest, Darabos et al. [26] compared IL-1β levels in the synovial fluid (SF) of 10 patients treated with IL-1-Ra to 10 patients treated with placebo (physiological saline) following ACL reconstruction surgery. Surgery caused an immediate elevation of synovial fluid concentration of IL-1β levels in almost all patients (19 of 20). After 10 days, patients treated with IL-1-Ra had concentrations that were equal to or below the concentration in a normal knee and statistically lower than placebo. The authors concluded that the dramatic decrease in IL-1β facilitated by IL-1-Ra application could augment the ACL healing process. The same authors confirmed these results in a larger trial (n = 62) and observed several postoperative outcomes associated with IL-1β concentrations [27]. The most important finding was the significant reduction in bone tunnel widening in autologous conditioned serum (ACS) treated patients at 6- and 12 months. Treated patients had significantly fewer joint effusions and performed better on functional tests at 6 months and had significantly greater range of motion at 12 months. Patient-administered outcomes (WOMAC and IKDC) were significantly improved in ACS-treated and placebo-treated groups; however, patients treated with ACS reported consistently lower pain scores and significantly improved WOMAC stiffness scores ($p = 0.047$) compared to placebo.

Treatment of OA continues to be a challenge for clinicians and investigators. As the population continues to age, a greater percentage of the population will likely develop OA and require surgical intervention unless a disease modifying drug is developed. To date, the Osteoarthritis Society International (OARSI) [30] and European League against Rheumatism [31] recommend acetaminophen as the first choice of oral analgesics to treat mild-moderate knee OA, and if successful, should be used as the preferred long-term analgesic due to its efficacy, relative safety and low cost. However, the evidence suggests that NSAIDs are superior to acetaminophen for improving knee pain in people with OA [32] and should be administered to patients who do not respond to acetaminophen [30,33–35] or as an initial therapy option for patients with moderate to severe pain [2,36]. Despite the superior clinical response, NSAIDs should be used with caution due to the well documented serious gastro-intestinal, renal and cardiovascular toxicities [37] including the FDA warnings about stroke and myocardial infarction. Another recommended treatment option includes the short-term use of IA corticosteroid injections [35]; however, similar to NSAIDs treatment, serious potential side effects of long term administration abound [38]. Since knee OA is a chronic disease, these short term treatment options highlight the significant unmet need for a disease-modifying OA drug that does not have any major side effects.

## 5. Conclusions

Our novel process to induce extremely high levels of the potent receptor antagonist for IL-1 requires a short incubation time to allow same day, point of care service to patients, utilizing a closed loop system to reduce the risk of contamination, and does not introduce any additional chemicals to the biotherapeutic product. Extremely high levels of IL-1-Ra are consistently achieved without augmenting key pro-inflammatory cytokines. Additionally, it is relatively inexpensive and can be safely stored without degrading IL-1-Ra or compromising the IL-1-Ra:IL-1β block. A large, well-designed, randomized clinical trial is needed to assess the symptom relief and chondroprotective effects of IL-1-Ra. Meanwhile, the Arthrokinex™ conditioning process offers an alternative, point of service molecular approach to rapidly induce IL-1-Ra which has the potential to provide therapeutic benefit in the treatment of mild to moderate OA.

## Disclosure statement

The research being reported in this publication was supported by Memorial Clinical Research, a division of Barreto Healthcare Clinic. Angelique Barreto has equity ownership in, serves as an advisor for, serves on the board of directors of Arthrokinex Joint Health LLC., which is developing a process related to the research being reported. The terms of this arrangement have been reported to the IRB. Timothy Braun is not affiliated with Memorial Clinical Research and reports no conflicts of interest.

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ARTHROKINEX
JOINT HEALTH

# CLINICAL EDUCATION GUIDE

AN INTRODUCTION TO OSTEOARTHRITIS

# A NATION IN PAIN

*More than 27 million Americans are affected by Osteoarthritis. Those who are affected commonly experience joint pain and stiffness. Sufferers report that it negatively affects their quality of life, and say that they often find it difficult to perform basic tasks such as climbing tasks or doing basic housework.*

Osteoarthritis is a disease of the entire joint involving the cartilage, joint lining, ligaments, and underlying bone. The breakdown of these tissues eventually leads to pain and joint stiffness. Among the joints most commonly affected are the knees, shoulders, hips and back.

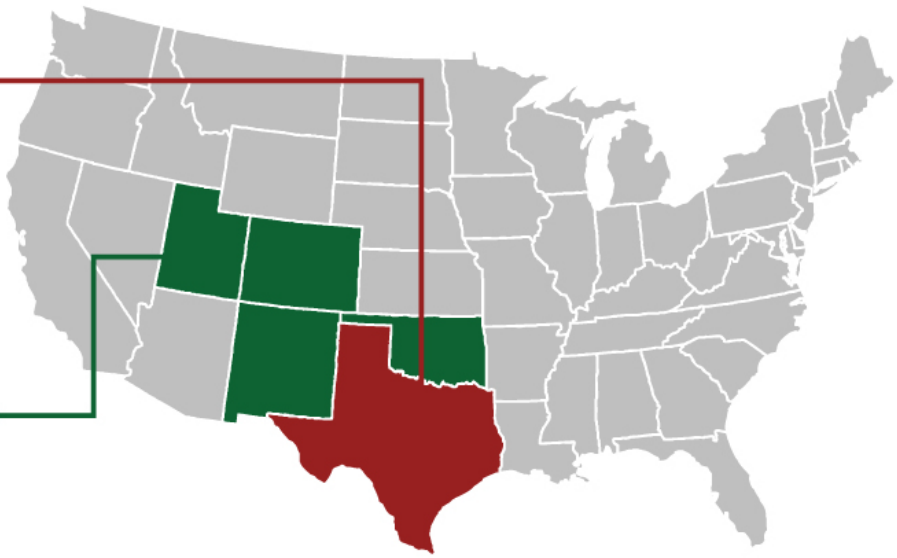
The specific causes of osteoarthritis are unknown, but are believed to be a result of both mechanical and molecular events in the affected joint. Disease onset is gradual and typically begins at age 40, though symptoms can sometimes manifest as early as age 25.

Osteoarthritis affects people in different ways, though pain and stiffness are the two most commonly reported symptoms. Other effects of osteoarthritis include depression, anxiety, feelings of helplessness, limitations on daily activities, job limitations and difficulty performing everyday personal and family joys and responsibilities.

The disease also often has financial repercussions in the form of lost wages (due to the inability to work) and treatment costs.

## INFOGRAPHIC: Understanding the Scope of Osteoarthritis.

- Osteoarthritis - the most common form of arthritis - affects **26.9 million** Americans, a group that is slightly larger than the population of Texas.
- 1 in 3 adults (33.6%) aged 65 and older is affected by osteoarthritis. That's more than **12.4 million** people, roughly equivalent to the combined populations of Utah, Colorado, New Mexico and Oklahoma.



THE ARTHOKINEX STORY

# WHY THIS PROGRAM WAS DEVELOPED

*We are experts in the treatment of inflammation and joint pain. Our objective is to help Americans afflicted with osteoarthritis take back their lives - one patient at a time.*

Our mission is to provide natural, rapid and lasting joint pain relief with a revolutionary and comprehensive treatment for total wellness, and without reliance on surgery or opiate painkillers. We are proud to say that we've helped hundreds of patients improve their quality of life through our natural, evidence-based program.

Regenerative treatment, like Arthrokinex used to require overseas travel, and was once something that only the ultra-wealthy - including professional athletes like Kobe Bryant - could afford.

But today, a unique treatment is not only available within the United States, it is available to hard-working Americans like you.

We opened our first Center in Oklahoma City, Oklahoma, in 2013 with the goal of delivering patient-centered care with a focus on total health and well-being. With our one-of-a-kind treatment model, we experienced rapid growth - in part because this aspect of pain management has been largely ignored in traditional medical practice.

Since then, we have opened a second joint pain center in Austin, Texas, and are currently in the process of expanding nationwide.

*Osteoarthritis is a complex disease and each person's treatment needs are unique. We provide innovative, cutting-edge treatment in a nurturing environment.*

OUR 12 MONTH PROGRAM

# PHYSICIAN-DIRECTED TREATMENT


*Treatment includes dedicated one-on-one time with our Arthrokinex physician, who will:*

- Perform the Arthrokinex procedure (see details on following page)
- Conduct follow-up visits and treatments
- Place physical therapy orders if needed
- Utilize TENS (trans-cutaneous electrical nerve stimulation) machines to treat pain if needed
- Evaluate bone health
- Prescribe medication and nutritional supplements as needed

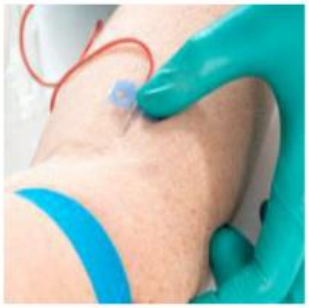
Our physician-directed treatment program is designed to help you achieve total joint wellness.

THE ARTHROKINEX INJECTION PROCEDURE

# THE FOUNDATION OF PERSONALIZED TREATMENT

*An initial evaluation of your joint is completed with the help of basic imaging and lab work to assess if the program would be of help to you. If you are eligible, a series of Arthrokinex injections will be started to help your pain and mobility.*

These visits take less than an hour and are relatively painless. The procedure is performed in our physician's office, and does not require anesthesia or an overnight hospital stay.



## STEP 1

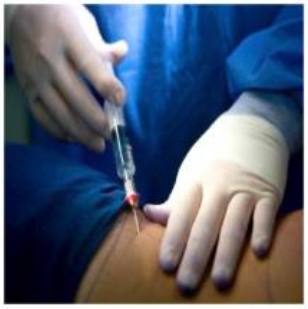
Removal of your blood from your vein.

## STEP 3

The Arthrokinex (IL-1 Ra) serum is drawn into six sterile single-injection syringes.

## STEP 2

The separation process extracting Arthrokinex (IL-1 Ra) from whole blood in higher concentrations ON SITE.



## STEP 4

The first of six injections of Arthrokinex (IL-1 Ra) can be immediately introduced into the affected joint and other areas by a provider within 1 to 2 hours.

The usual protocol is a series of six injections delivered into one joint, over a one year period. The injections are used in combination with an anti-inflammatory diet and targeted dietary supplements as part of a comprehensive joint health program. The results speak for themselves: most of our patients experience a noticeable reduction in joint pain in a months time, and following the Arthrokinex program, in most cases can keep the patient's pain under control for a year or longer.

ARTHROKINEX PROGRAM TOOLS

# ACHIEVING TOTAL JOINT WELLNESS

*The Arthrokinex Joint Health program complements the Arthrokinex Injection procedure to provide you with a long-term solution to your joint pain.*

Though the underlying cause of osteoarthritis often cannot be cured, making lifestyle changes can have a positive impact on arthritis.

Lifestyle changes such as diet, exercise & supplements can help relieve stiffness, reduce pain and fatigue, and improve muscle and bone strength.

*Featured below are some of the key areas we'll address as part of the Arthrokinex Joint Health Program.*

**DIET & NUTRITION**
Nutrition plans, nutritional supplementation, osteoarthritis friendly recipes, healthy food preparation

**FITNESS & EXERCISE**
Personalized fitness plan, workout instruction, key exercises

**MEDICATIONS & SUPPLEMENTS**
Medicines and supplements may be prescribed along with lifestyle changes

**BEHAVIOR MODIFICATION**
Improving basic habits, such as sleep schedule, changing sedentary lifestyle, smoking cessation, and more

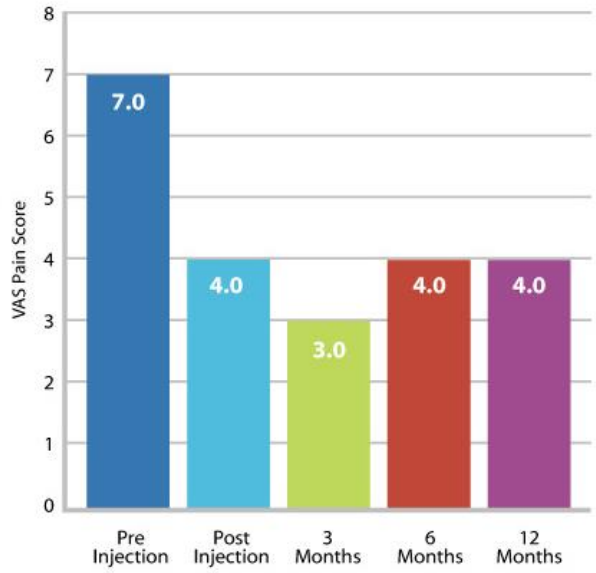
**SOCIAL SUPPORT**
Maintaining a healthy lifestyle with support from family and friends

OUTCOMES YOU CAN EXPECT

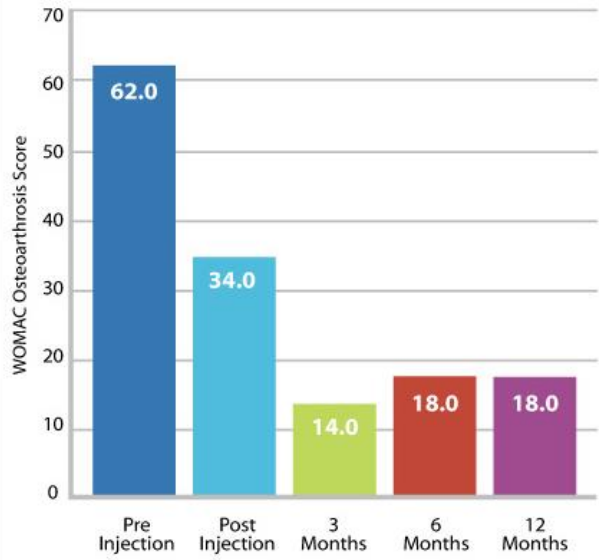
# METRICS THAT MATTER

*Starting in 2012, several patients of both genders and a variety of ages have successfully completed the Arthrokinex™ Joint Health Program. The pain scores and quality of life scores for all patients reduced dramatically almost immediately and continued benefit was reported at 3 month intervals up to a year later. Their clinical results and significant improvement are clearly seen in the graphs below:*

Comparison of VAS Pain Scores in Patients Before and After Arthrokinex™ Treatment




Comparison of WOMAC Osteoarthritis Scores in Patients Before and After Arthrokinex™ Treatment




# PATIENT STORIES

"Since I had the injection therapy my knee has been feeling much better. I walk like a normal person. I don't have to pull my leg like I used to."

*- Leyda H. - 65 yrs, Retired Attorney*

"Before the shots, (my knee) really hurt, especially when walking. I have no pain in my knee now. It is a blessing to have gotten rid of that pain."

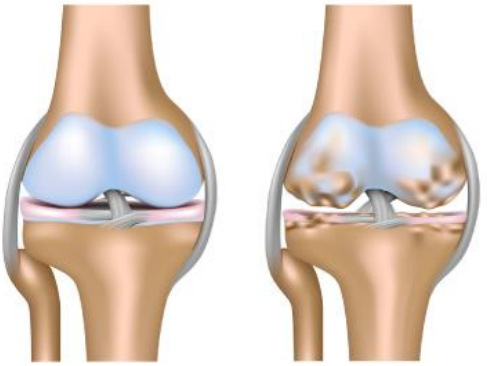
*- Suzanna G. - 63 yrs, Retired Oil & Gas Accountant*

"Arthrokinex has been a great addition to the treatment of arthritis. Wherever a corticosteroid injection is being given to patients, this should be considered instead."

*- Calvin Johnson MD., Orthopedic Surgeon*

ARTHROKINEX

# KNEE PROGRAM



Healthy knee joint  Osteoarthritis

Osteoarthritis is the most common cause of musculoskeletal pain and disability in the knee joint. In the knee joint, the end of the femur (thigh bone) and tibia (shin bone) are covered in smooth articulate cartilage. Between the two bones sits a second type of cartilage, called menisci, which act as cartilage shock absorber pads. Joint fluid also adds lubrication to the knee joint.

Osteoarthritis (OA) starts as the lack or loss of this articulate (surface) cartilage and then progresses into involvement with the surrounding bone, tissues, and synovial fluid. In osteoarthritis, cartilage may have areas of partial thickness loss (thinning) or complete loss of surface cartilage resulting in areas of exposed bone. Isolated cartilage loss may be a result of isolated trauma or it may be a result of chronic wear and tear of the joint.

Risk factors for OA include age, injury, anatomic joint abnormalities, heredity, high bone mineral density, joint hypermobility, obesity, muscle weakness, and overuse or under use of the joints.

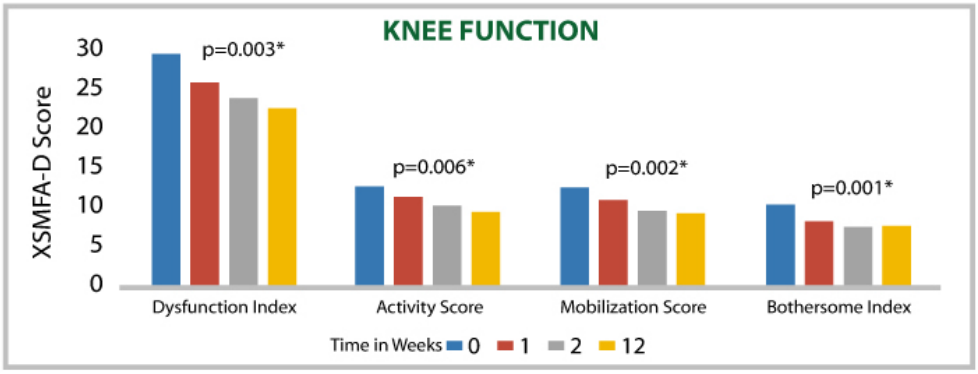
Symptoms of osteoarthritis include joint pain with activity, night pain, morning stiffness, limited motion, joint inflammation, crepitus or noise from the knee, and deformity.

# PHYSICIAN TESTIMONIAL


"I have researched intensively for an alternative to total knee replacement, as I have almost no cartilage in either knee as a result of previous surgeries. As the years have passed my pain has increased with my research for alternative treatment.

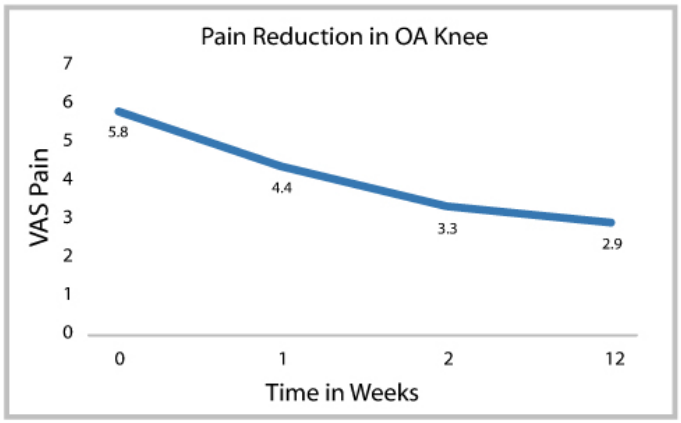
I am now finishing my 3rd injection from Dr. Barreto and the pain has decreased remarkably. While all patients may not experience the same relief... ***this should be mandatory therapy before having knee replacement surgery."***

*- Dale Massad MD., Occupational Medicine*

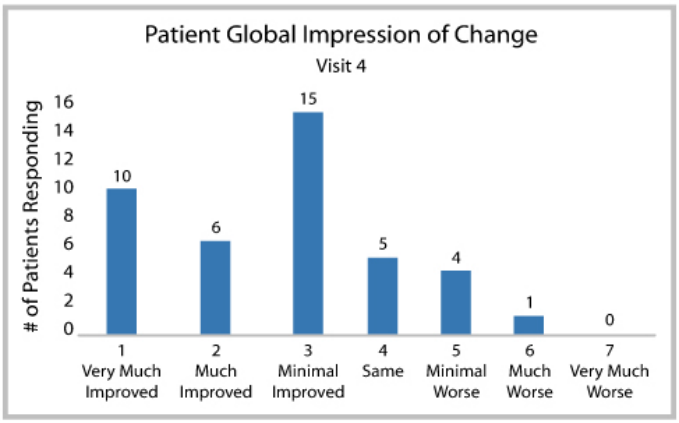



*Wilcoxon signed-ranked test comparing baseline to 2 weeks

*Compared to baseline, a robust and statistically significant improvement in each knee function subscale is observed in knee OA patients.*




Patients report a progressive and consistent reduction in knee ($p<0.001$) pain following joint injections of Arthrokinex.




Overall, 71% of the participants report an improvement in symptoms within 4 weeks and 76% report improvement over the next months.

# PATIENT STORIES

"As a firefighter, Arthrokinex has helped me to do my job pain free. I'm also able to do the activities I enjoyed when I was younger, such as basketball and volleyball."

*- Joe G. - 40 yrs, Firefighter*

"Prior to the injections, I had to climb stairs one step at a time, and it was very painful. Now I can climb stairs almost pain free. It was also very painful getting up from a low chair. I can now get down on the floor and get up. I thank God every day for Dr.Barreto and for the things she has done. I feel like a new person.

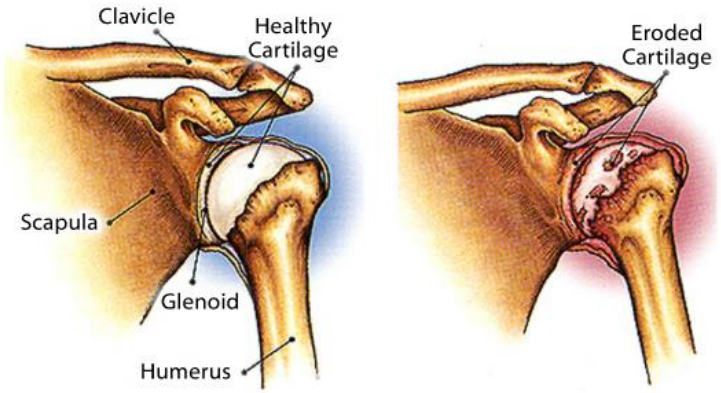
*- Norma L. - 77 yrs, Retired Nursing Staff*

"Following my 65th birthday, I became totally inactive due to extreme arthritis. I had to use a cane or walker. Immediately following the first injection, I had amazing relief from my pain and was able to walk without my brace or cane back to my automobile. The injection was not painful. I thank Dr. Barreto for giving me hope and a chance to walk again.

*- Gina J. - 65 yrs, Retired Dance Instructor*

ARTHROKINEX

# SHOULDER PROGRAM




Healthy Shoulder

Arthritic Shoulder

Your shoulder is made up of three bones: your upper arm bone (humerus), your shoulder blade (scapula), and your collarbone (clavicle). The head of your upper arm bone fits into a rounded socket in your shoulder blade. This socket is called the glenoid. A combination of muscles and tendons keep your arm bone centered in your shoulder socket. These tissues are called the rotator cuff.

There are two joints in the shoulder, and both may be affected by arthritis. One joint is located where the clavicle meets the tip of the shoulder blade (acromion). This is called the acromioclavicular (AC) joint. Where the head of the humerus fits into the scapula is called the glenohumeral joint.

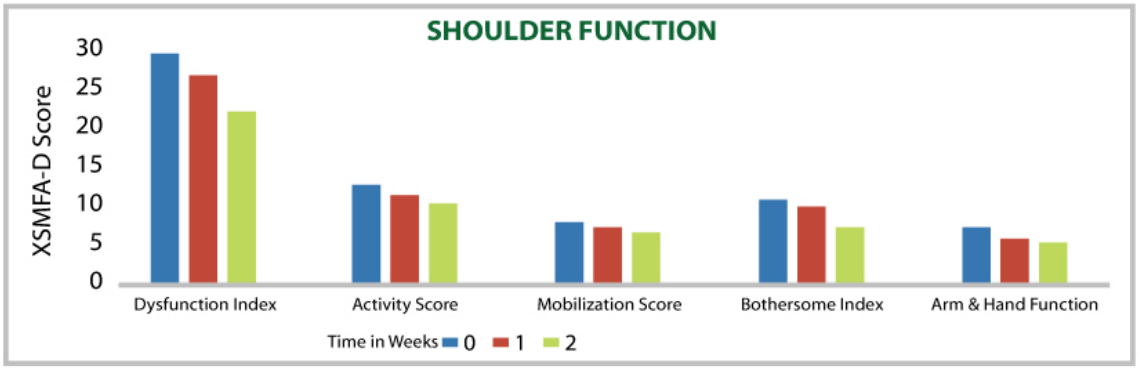
Also known as "wear-and-tear" arthritis, osteoarthritis is a condition that destroys the smooth outer covering (articular cartilage) of bone. As the cartilage wears away, it becomes frayed and rough, and the protective space between the bones decreases. During movement, the bones of the joint rub against each other, causing pain. Osteoarthritis commonly affects people over 50 years of age and is more common in the acromioclavicular joint than in the glenohumeral shoulder joint.

There are many risk factors for shoulder osteoarthritis, including age, genetics, sex, weight, joint infection, history of shoulder dislocation, and previous injury. Certain occupations, such as heavy construction or overhead sports, are also risk factors. The prevalence of shoulder osteoarthritis is increasing as the population ages.

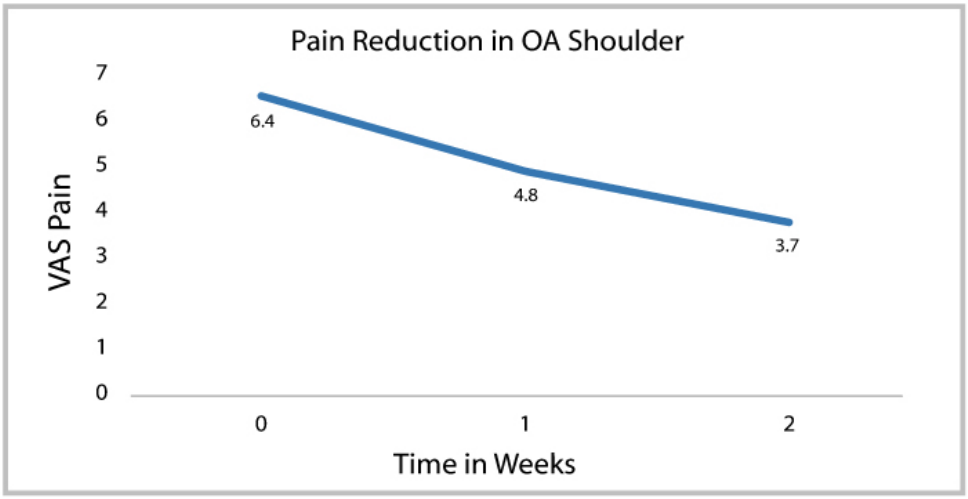
# PHYSICIAN TESTIMONIAL


"I have significant osteoarthritis in my left shoulder, and have successfully managed to postpone surgery using Arthrokinex Joint Injections. My shoulder pain is much better and I have been able to postpone surgery so far. As a pain management physician it is good to have an alternative, natural therapy to offer patients.

*- Stephen Blake Kelly MD.,*
*Specialist in Pain Management*




*Compared to baseline, a robust and statistically significant improvement in each shoulder function subscale is observed in shoulder OA patients.*




Patients report a progressive and consistent reduction in shoulder ($p<0.002$) pain following IA injections of Arthrokinex.

# PATIENT STORIES

"The injections worked! I noticed an immediate change after my first injection. My pain level and stiffness decreased. My ability to move was greatly increased. I received greater improvement with each injection. I could not have asked for a better treatment plan. "

*- Nancy G. - 52 yrs, School Teacher*

"Until I joined the Arthrokinex Joint Health Program I was unable to play with my grandchildren without pain. I am able to move better and able to spend good quality time with my family. I would recommend the program to anyone considering it."

*- Shirley H. - 67 yrs, Retired Realtor*

"The Arthrokinex Joint Health Program has helped me to enjoy life again. I am able to go back to the gym and exercise without pain. I have lost 18 pounds and overall feel better. I have improved my range of motion in my shoulders and am able to lift objects allowing me to do daily functional activities."

*- Roy P. - 53 yrs, Investment Banker*

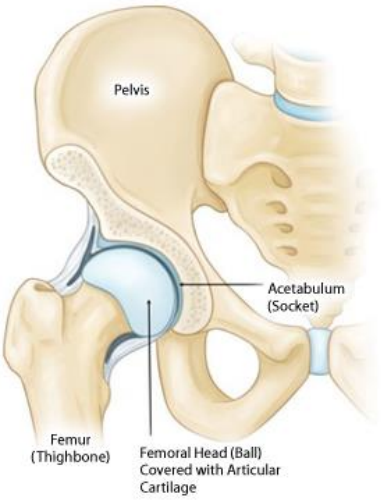
ARTHROKINEX

# HIP PROGRAM

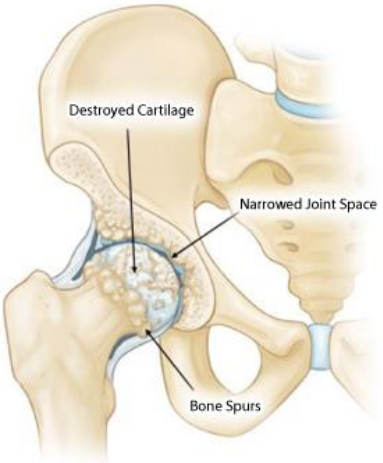
Osteoarthritis of the hip has no single specific cause, but there are certain factors that may make you more likely to develop the disease, including increasing age, family history of osteoarthritis, previous injury to the hip joint, Obesity and improper formation of the hip joint at birth, a condition known as developmental dysplasia of the hip. Unfortunately, even if you do not have any of the risk factors listed above, you can still develop osteoarthritis of the hip.

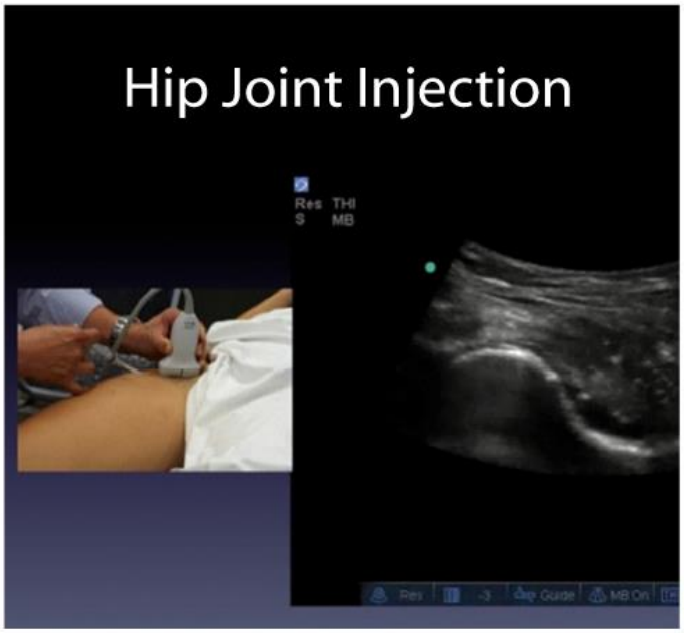
The most common symptom of hip osteoarthritis is pain around the hip joint. Usually, the pain develops slowly and worsens over time, although sudden onset is also possible. Pain and stiffness may be worse in the morning, or after sitting or resting for a while. Over time, painful symptoms may occur more frequently, including during rest or at night. Additional symptoms may include "Locking" or "sticking" of the joint, and a grinding noise (crepitus) during movement caused by loose fragments of cartilage and other tissue interfering with the smooth motion of the hip, decreased range of motion in the hip that affects the ability to walk and may cause a limp and increased joint pain with rainy weather.

*Normal Hip Anatomy*

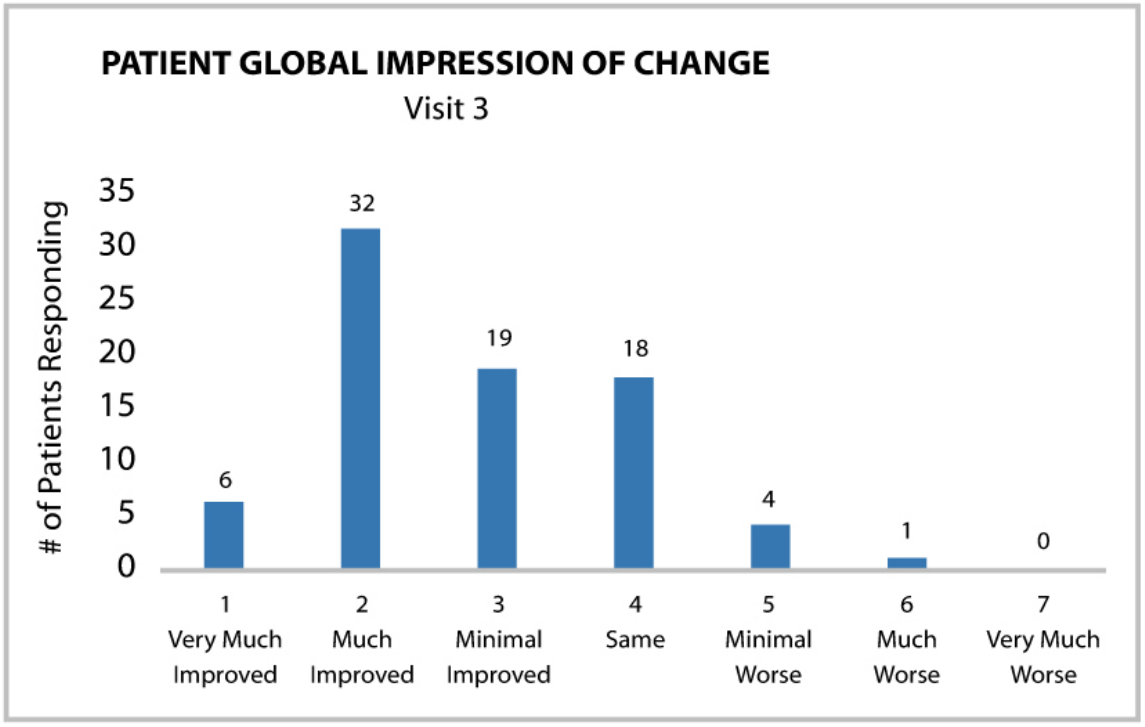



*A hip damaged by Osteoarthritis*




The hip is one of the body's largest joints. It is a "ball-and-socket" joint. The socket is formed by the acetabulum, which is part of the large pelvis bone. The ball is the femoral head, which is the upper end of the femur (thighbone). The bone surfaces of the ball and socket are covered with articular cartilage, a smooth, slippery substance that protects and cushions the bones and enables them to move easily. The surface of the joint is covered by a thin lining called the synovium. In a healthy hip, the synovium produces a small amount of fluid that lubricates the cartilage and aids in movement.




*71% of patients in the Arthrokinex Program report noticeable improvement.*

# PATIENT STORIES

"Dr. Barreto is outstanding, her ability to do the ultrasound guided injections are incredible. My pain is now manageable. The whole experience has been a pleasure. I would say a top notch experience."

*- Jim D. - 73 yrs, Retired Marine Core, Naval Aviator*

"The Arthrokinex injection therapy significantly improved my overall quality of life. I was able to get back to the activities I enjoy with absolutely no pain."

*- Elizabeth N. - 56 yrs, Licensed Clinical Social Worker*

"When the injections were received it relieved muscle cramping and tension allowing for greater mobility in my lower back and legs. I had prior back surgery and wanted to delay another. Dr. Barreto did a great job with the ultrasound procedure. Dr. Barreto and her staff were concerned and caring.

*- Jody B. - 62 yrs, Commercial Banker*

"I highly recommend Dr. Barreto and the Arthrokinex program. Arthrokinex injections have helped with my arthritic knee pain and they have delayed the need for surgery. When Dr. Barreto used the ultrasound guided needle for the injections, I felt confident that the Arthrokinex serum was placed exactly where it needed to be. It was interesting to see the placement process. Further, part of the success of the Arthrokinex treatment comes from the kind, caring, and thorough practice style shown by Dr. Barreto towards her patients. She teaches patients about overall wellness such as food choices, medications, and exercise for arthritis setting the stage with some preventive and strengthening measures that can be done by the patient. This caring practice style is well emulated by her staff members. Again, I highly recommend Dr. Barreto and the Arthrokinex process!

*- Beverly M. - 71 yrs, Health Care Consultant*

ARTHROKINEX

# FREQUENTLY ASKED QUESTIONS

**Q. What is Arthrokinex IL-1-Ra?**

**A.** Arthrokinex IL-1-Ra harnesses the body's own natural healing ability, also known as Autologous Conditioned Serum (ACS). A phlebotomist takes 60ml of your own blood, the blood is incubated for 1 hour and then the blood is spun in a centrifuge. The results are a concentration of an anti-inflammatory protein called an interleukin-1 (IL1) antagonist and growth factors (GF's). A series of 6 syringes are then filled with the concentration that will be injected into the patient over a one year period. The first 3 are one week apart and the other injections are three months apart.

**Q. How does it work?**

**A.** This concentration of the IL1 antagonist and GF's have the capability to decrease the inflammation of an arthritic joint and attempt to decrease the natural advancement of the arthritis. The result is improved function and decreased pain. An orthopedic surgeon is usually reluctant to offer a replacement on a patient with mild to moderate arthritis, even if the patient is having pain. Arthrokinex is an option for patients who are in this category.

**Q. Who is this treatment for?**

**A.** Patients with mild to moderately severe osteoarthritis who:

- are not appropriate for replacement surgery or wish to postpone surgery if possible
- are needing an improvement in function
- have pain that is difficult to live with
- have failed previous treatments including physical therapy and other joint injections such as cortisone or synvisc

**Q. How long does the beneficial effect of the treatment therapy last?**

**A.** The average duration of benefit in studies is so far about 1 to 1.5 years, but published European studies indicate that patients may benefit even longer from Interleukin IL 1 Ra injections.

**Q. I have heard of PRP therapy - how is Arthrokinex different to PRP therapy?**

**A.** PRP is similar where your blood is taken and spun down, but usually is only for one injection for tendons. PRP is not as effective as Arthrokinex is in joints due to not having the anti-inflammatory proteins (IL1). It also has decreased growth factors. So Arthrokinex is much more effective in providing more rapid relief.

**Q. Do I need a Doctors referral?**

**A.** Not unless it is required by your insurance company.

**Q. How often do I have to come?**

**A.** If you live close to the clinic, the ideal approach is initially 1 injection per week for 3 weeks. Thereafter, you will return every three months for the maintenance doses totaling 3 additional injections. All injections are done using ultrasound guidance for accuracy in the procedure.

If you are from out of town you have the option of getting the first three injections one day apart. Your blood will be drawn on day one and you will come back later that day for your first injection. You can then stay at a local hotel the next two days to receive injections two and three. You will then come back every three months for the maintenance doses totaling 3 additional injections. This option can be discussed at the time of the consultation with the physician.

**Q. What are the risks and is the injection accurately guided into the joint?**

**A.** All injections are guided by an ultrasound for accuracy. There are minimal risks to the procedure since it is your own blood being injected back into you. All equipment used is FDA approved and all injections are prepared and delivered via an aseptic technique. Joint injection site risk is minimal, as with any type of joint injection. The research has demonstrated minimal risk if any.

**Q. What are the anticipated results?**

**A.** Anticipated results can vary from a significant decrease in pain to a complete resolution of pain. There have been several reputable studies to confirm these changes in joints with arthritis. As with most procedures, results are not 100% guaranteed. Still, there is a strong chance you will benefit from Arthrokinex Joint Health Program where other therapies were unsuccessful. A few patients (less than 1.5%) reported elevated pain levels after the first injection which disappeared spontaneously. All the injections are completed on an outpatient basis, in the office, using ultrasound guidance technology to ensure minimal pain and lessen damage to surrounding tissues.

**Q. What happens after my 6 injections?**

**A.** You will be given several pain assessment sheets to fill out at every visit so we may assess your response to Arthrokinex. The physician may also recommend you see a physical therapist who specializes in this type of treatment and who may work with the physician. Alternatively, if you have your own physical therapist, they will be given strict procedures for the rehabilitation process.

**Q. Can I repeat the Arthrokinex Joint Health Program?**

**A.** The Arthrokinex Joint Health Program is a purely natural biologic treatment produced from the patient's own blood. It contains NO ANALGESICS, STEROIDS or ADDITIVES. As such, there is no restriction in repeating the treatment.

**Q. Can I continue with my sports and daily activities while undergoing the biological treatment?**

**A.** Based on the experiences of Arthrokinex™ Joint Health Program patients, there are no restrictions in physical activity induced by the therapy. In fact, certain exercises are found to be beneficial to the treatment by improving joint function and stability.

**Q. How often may I repeat the Arthrokinex Joint Health Program?**

**A.** There are no restrictions on the number of treatment series as long as they remain effective for patients.

**Q. Do clinical studies confirm the beneficial effects of the Arthrokinex Joint Health Program?**

**A.** Since 2012, several hundred Ultrasound Guided Joint Injections have been completed at our center. The majority of our patients, of various backgrounds and ages, achieve tangible and measurable pain relief. There are over five clinical studies to date on Interleukin IL 1 Ra joint injections demonstrating their efficacy, safety and long term benefits for osteoarthritic knees, hips, spine, chronic tendonosis, and muscle strains.

**Q. I am on a "blood thinner." Can I still do the Arthrokinex Joint Health Program?**

**A.** Yes, but some drugs may need to be changed before an injection therapy. A physician in our clinic will advise you, and you are encouraged to consult with your personal physician also.

**Q. Can I combine the Arthrokinex Joint Health Program with other therapies?**

**A.** The Arthrokinex Joint Health Program is a comprehensive plan combining an anti-inflammatory diet, relevant supplements, exercise and physical therapy recommendations to complement the positive effect of the natural injections and enhance pain reduction and joint mobility.

**Q. What cost is involved with the Arthrokinex Joint Health Program?**

**A.** The cost to prepare 6 joint injections is nominal. Comparative therapies range from $800 to $5,000 PER injection. The patient is responsible for all of their co-pays, deductibles and out-of-pocket maximums. Financing options are available for the nominal cost of preparing the injections and this can be discussed at the time of the consultation. The program consists of seven office visits, six ultrasound guided injections, a customized diet plan, education on exercise techniques, and monitoring of the level of your pain.

**Q. What is the process to set up a consultation to undergo the Arthrokinex Program?**

**A.** You need to schedule an appointment with an Arthrokinex trained physician by scheduling an appointment through the website (www.arthrokinex.com) or by calling 1-855-956-1377. You will be scheduled to have comprehensive laboratory and x-rays performed and once these results have been received, you will be scheduled for a consultation to determine if the Arthrokinex Joint Health program is beneficial to you.

# ARTHROKINEX
JOINT HEALTH

***- FEATURED ON FOX25, MAY 2014***


A medical breakthrough in Oklahoma City is offering relief to those suffering from osteoarthritis. Pain is treated with the body's own anti-inflammatory proteins. Essentially the body heals itself, allowing patients to avoid or put off major surgery. "I enjoy driving the fire engine," said OKC firefighter Walter Hawkins. "I enjoy that. I love being out in the field." Hawkins' arthritis in his knees got so bad, it threatened to take him off the front lines. "It got to the point I couldn't stay on it very long," said Hawkins. "It hurt to mow the yard. It hurt to workout." Not ready for major knee replacement surgery, Hawkins turned to a brand new option called Arthrokinex.

Dr. Angelique Barreto used an ultrasound to pinpoint exactly the area causing Hawkins' pain.

*"That's exactly where I'm going to place your injection," she said. The injection comes from Hawkins' own body. Blood is taken from the vein, then immediately put through a separation process, creating a highly concentrated liquid full of the body's own anti-inflammatory proteins. We watched as the Arthrokinex was injected into Hawkins' joint pouch. One injection a week for several weeks should give him lasting pain relief.*

Another patient, Elizabeth Newell, said, "After the 2nd injection, my life changed."
It's been a year since Newell had the procedure on her knee.

"Any pain? any swelling?" Dr. Barreto asked her at a follow up appointment. "No," Newell answered. She couldn't tolerate the side effects of prescription anti-inflammatories. And the pain was robbing her quality of life. "My life was changing into a direction I was not happy with, because I was unable to do so many things."

Newell and Hawkins are among the hundred or so patients who have used Arthrokinex over the last few years as Dr. Barreto developed and perfected her patented process. She's able to offer the procedure for a fraction of the cost of her competitors in Germany. But for her patients, the relief they get is priceless.

"I want to get back to the karate school," said Hawkins. "I hadn't been in there in a while. I'm looking forward to getting back in there and working out."

Newell said, "This is natural. Your own body healing itself. How wonderful that is!"

*For more information, call (855)956-1377. You can also take a short quiz online at* ***https://www.arthrokinex.com****, to find out if you're a good candidate for Arthrokinex.*