

An intra-articular, extended-release formulation of triamcinolone acetonide as a cost-effective therapy for treating osteoarthritis of the knee



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INTRODUCTION

Background

- Osteoarthritis (OA) is a chronic disease caused by inflammation and breakdown of cartilage in the joints over time. OA affects over 30 million adults in the United States, and is one of the leading causes of disability¹
- OA has a detrimental affect on a patient's quality of life due to both pain and functional limitations
- Pain, functionality, and quality of life for OA patients can be measured using a variety of validated scales and instruments^{2,3}
- Non-surgical approaches to OA therapy included physical therapy, pain relievers, non-steroidal anti-inflammatories (NSAIDs), intra-articular steroid injections, and intra-articular hyaluronic acid (HA) injections⁴
- A new, extended release formulation of the corticosteroid triamcinolone acetonide (TA-ER) (FX006) has been developed as an intra-articular injection to provide extended joint residence time and enhanced pain relief from knee OA⁵
 - TA-ER is a suspension of microspheres consisting of TA embedded within a poly lactic co-glycolic acid (PLGA) copolymer mix to facilitate delayed release of TA⁵

Objective

- Utilize the clinical impact of TA-ER on pain, stiffness, and function to estimate impact on overall quality of life in knee OA
- Evaluate the potential cost-effectiveness of TA-ER as a knee OA therapy in comparison to existing therapies⁶

Study Population

- Pooled data from three Phase 2/Phase 3 randomized, controlled trials (NCT01487161, NCT02116972, and NCT02357459).
 - 324 patients received a single intra-articular injection of TA-ER (FX006 40 mg).
 - Treatment effectiveness compared to 262 patients who received a single intra-articular injection of saline placebo.
- Patient inclusion criteria for all the trials included the following:
 - Unilateral or bilateral OA diagnosis greater than 6 months; radiographic evidence of Kellgren-Lawrence Grade 2 or 3 OA
 - Male or female patients 40 years old or older
 - Qualifying mean 24 hour pain score and a body mass index of less than or equal to 40 kg/m²

Study Measures

- Clinical outcome measures included Western Ontario and McMaster University Arthritis Index for OA (WOMAC) assessments, including the subscores for WOMAC-A (Pain), WOMAC-B (Stiffness), and WOMAC-C (Function)³
- Improvement in quality of life was assessed by converting WOMAC scores to Health Utilities Index Mark 3 (HUI-3) scores using an established algorithm^{2,3}
 - HUI3 Score = 0.5274776 + 0.0079676 x Pain + 0.0065111 x Stiffness - 0.0059571 x Function + 0.0019928 x Pain x Stiffness + 0.0010734 x Pain x Function + 0.0001018 x Stiffness x Function - 0.0030813 x Pain² - 0.0016583 x Stiffness² - 0.0002430 x Function² + 0.0113565 x Age - 0.0000961 x Age² - 0.0172294 x Female - 0.0057865 x OA duration + 0.0001609 x OA duration²

Cost-Effectiveness Analyses

- Quality adjusted life years (QALYs) were estimated as a 6 month weighted average of mean HUI-3 gain from baseline, as described by Rosen *et al*⁶
- Existing knee OA medication (WAC) and therapy costs (including injection fees) for conventional care (CC), diclofenac, and average values for HA single and multiple injection agents were obtained from published literature and other sources⁷
- Incremental cost effectiveness ratios (ICERs) were calculated for TA-ER at a hypothetical price of \$500 versus existing therapies

RESULTS

Figure 1. Changes in the WOMAC-A (Pain), -B (Stiffness), and -C (Function) subscores following intra-articular administration of TA-ER. Panel A) WOMAC-A values; Panel B) WOMAC-B values; and Panel C) WOMAC-C values from baseline through week 24.

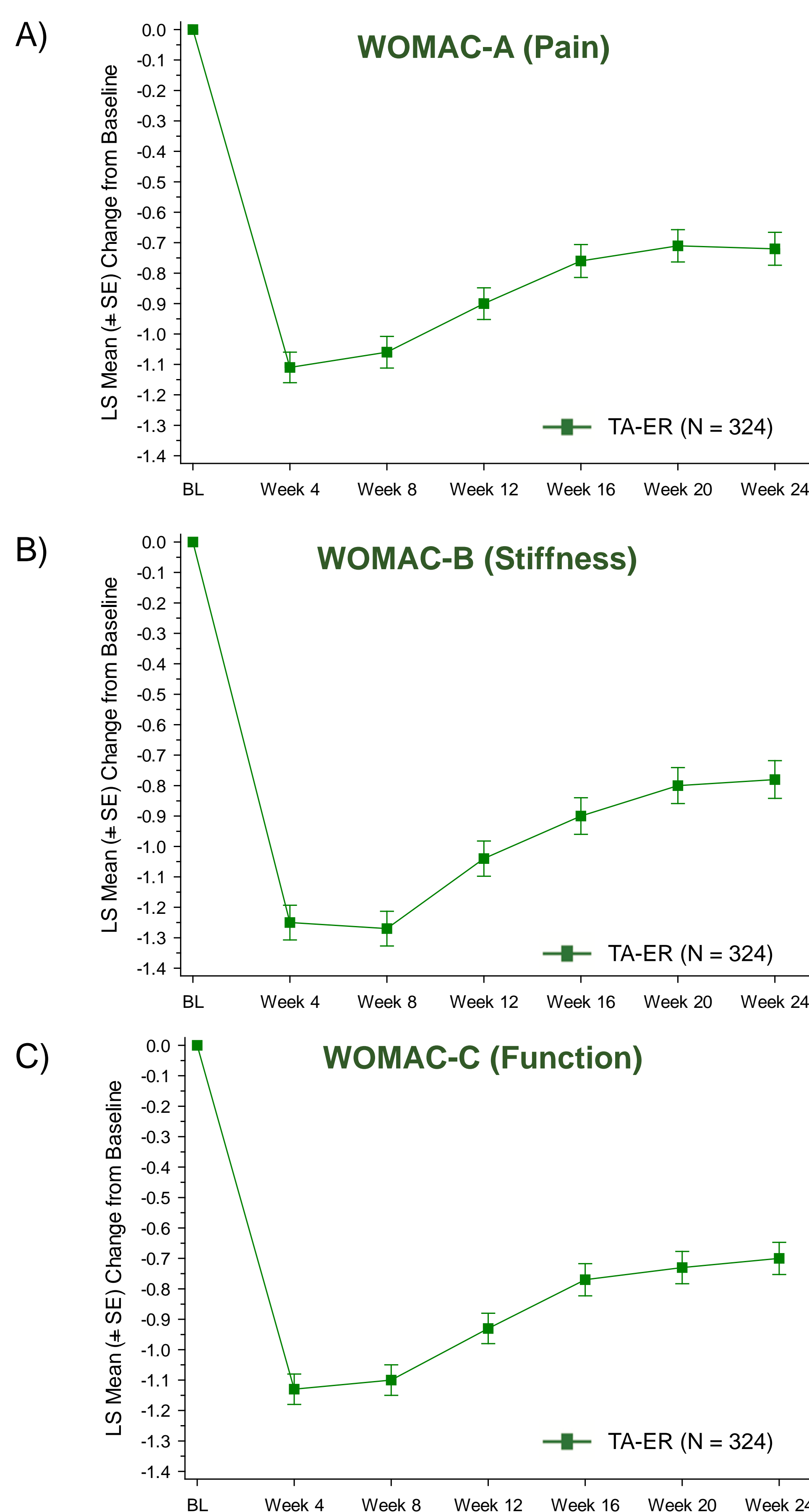


Figure 2. TA-ER administration results in substantial and sustained benefits versus placebo. The forest plot shows the WOMAC-A, -B, and -C subscores for TA-ER versus placebo.

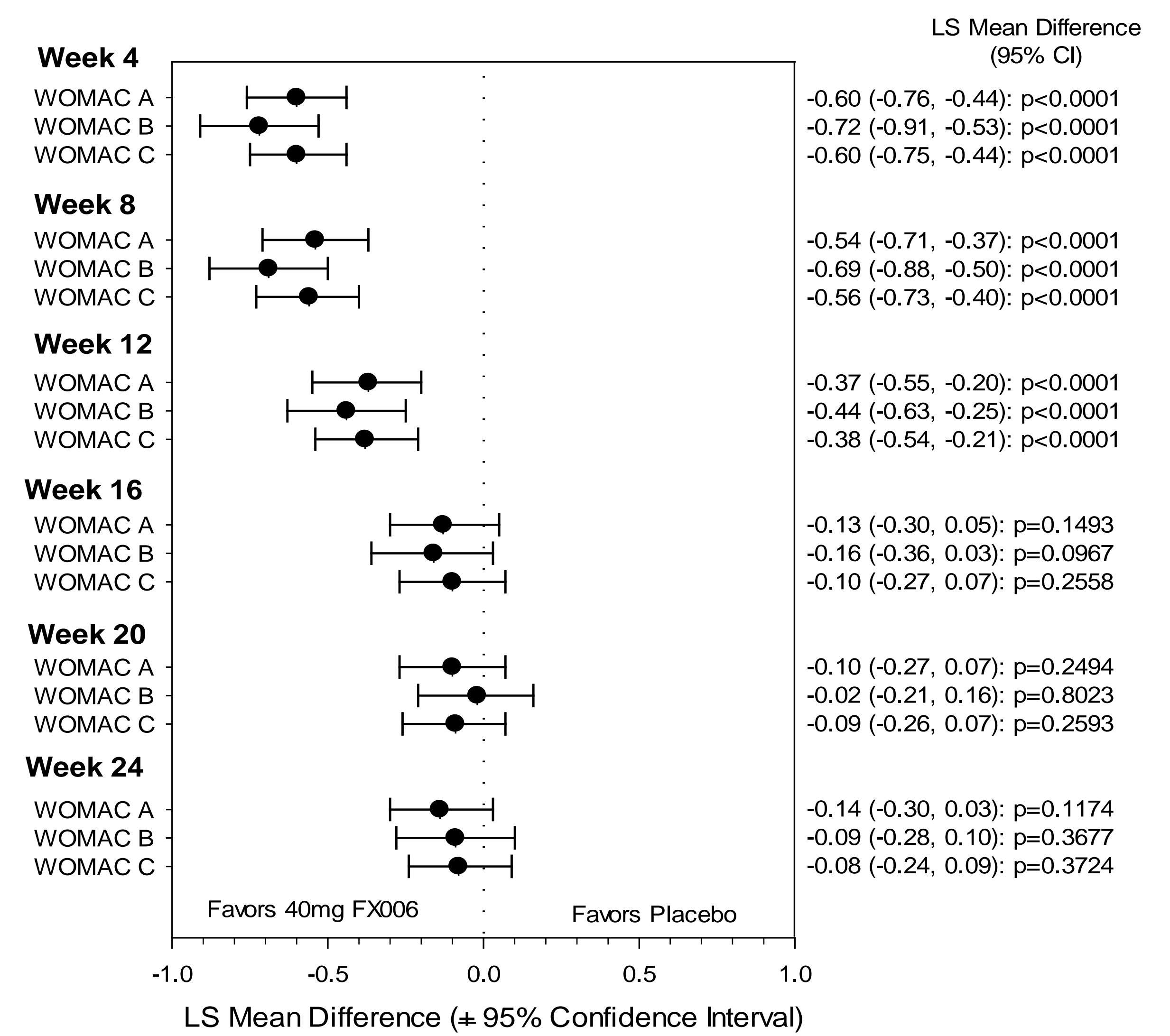
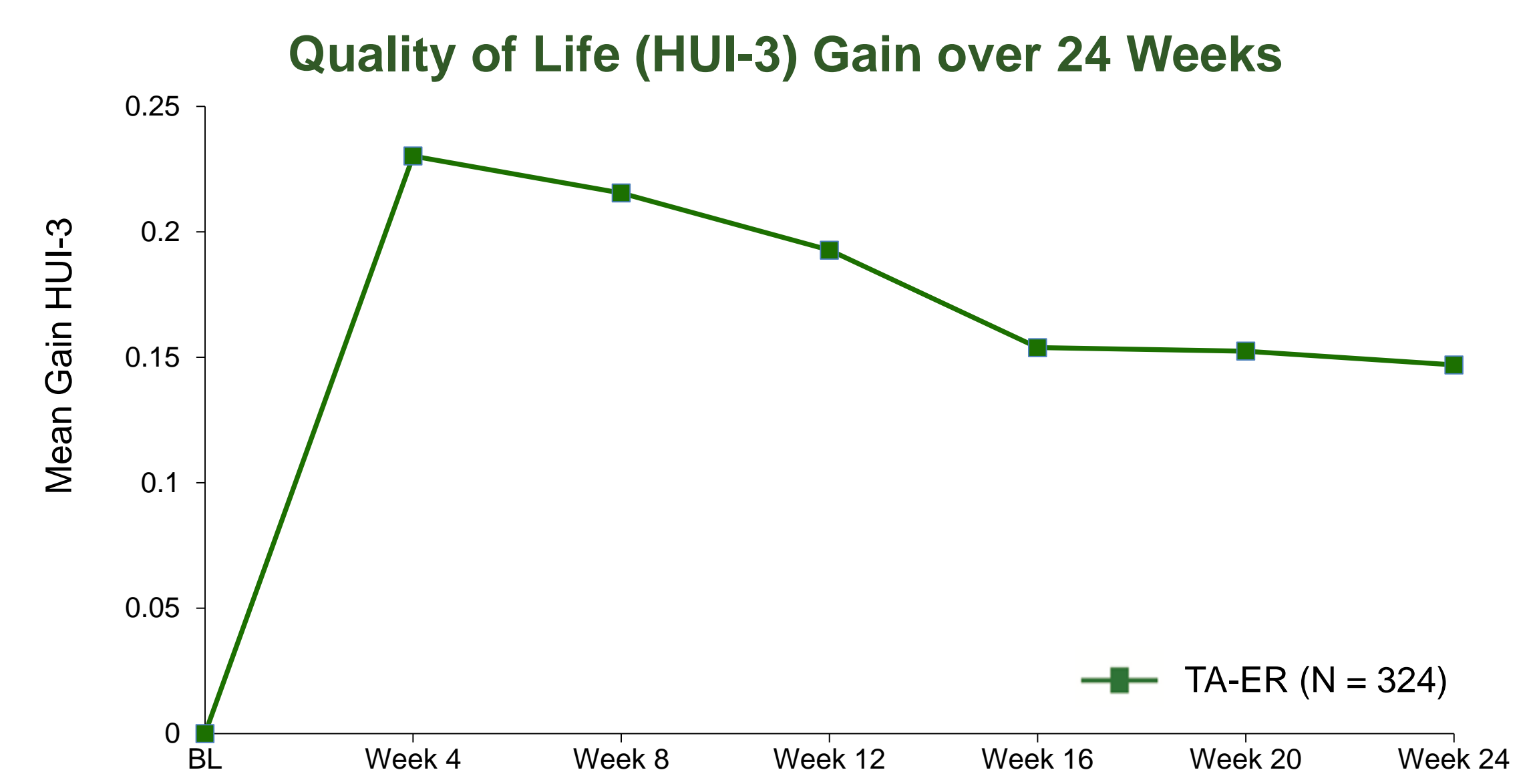


Figure 3. Treatment with TA-ER results in increases in HUI-3 from baseline. HUI-3 scores were calculated from WOMAC-A, -B, and -C scores for patients treated with TA-ER.



Economic Assessment of Managing Patients with Osteoarthritis

Drug and Treatment Costs

Treatment	Drug Cost ⁷	Treatment Cost ⁷
Conventional Care (CC)	N/A	\$ 322
Diclofenac	\$ 212	\$ 212
HA Average	\$ 1,091	\$ 1,459
TA-ER	\$ 500	\$ 605

Cost per QALY

Treatment	QALY (6 mo)	\$/QALY
Conventional Care (CC)	0.030	\$ 10,717
Diclofenac	0.078	\$ 2,708
HA Average	0.110	\$ 13,267
TA-ER	0.189	\$ 3,201

ICERs versus Other Therapies

Treatment	ICER vs. CC	ICER vs. Diclofenac	ICER vs. HA Average
Diclofenac	Dominant (-\$2,291)	-	-
HA Average	\$ 14,212	\$ 39,233	-
TA-ER	\$ 1,783	\$ 3,549	Dominant (-\$10,815)

Tables 1-3. Summary of the per-patient treatment costs, Cost per QALY, and ICERs vs other therapies. Drug cost and total cost of care for HA, conventional care (CC), and diclofenac are based on January 2017 Truven REDBOOK WAC pricing⁷ and Rosen *et al*.⁶

CONCLUSIONS

- Intra-articular TA-ER administration was associated with improvement from baseline status in pain, stiffness, and function over 24 weeks assessed by WOMAC measures. These effects were significant versus saline placebo effect over 12 weeks.
- The observed clinical benefits of TA-ER translated to an increase in quality of life for knee OA patients, as demonstrated by a maximal 0.229 point increase in the HUI3 of patients receiving TA-ER at 4 weeks post-injection
 - The average QALY gain per 6 months was 0.189
 - The cost per QALY gained was \$3,201
- At a hypothetical drug cost of \$500, TA-ER is a cost effective treatment, with ICERs of less than \$5,000 versus either conventional care or diclofenac
- In ICER analysis versus intra-articular HA, TA-ER was the dominant approach

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