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MEETING ABSTRACTS

A Multi-Center Double-Blind, Randomized, Controlled Trial (db-RCT) to Evaluate the Effectiveness and Safety of Co-Administered Traumeel® (Tr14) and Zeel® (Ze14) Intra-articular (IA) Injections Versus IA Placebo in Patients with Moderate-to-Severe Pain Associated with OA of the Knee

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Carlos Lozada[1], Eve del Rio[2], Donald Reitberg[2], Robert Smith[2], Charles Kahn[3] and Roland W. Moskowitz[4], [1]Rheumatology, University of Miami Miller School of Medicine, Miami, FL, Miami, FL, [2]Clinical Research, Rio Pharmaceutical Services, LLC, Bridgewater, NJ, [3]South Florida Rheumatology, Hollywood, FL, [4]Div of Rheum/Dept of Medicine, University Hospitals Case Medical Center, Cleveland, OH

Background/Purpose:
Tr14 & Ze14 is a combination of dilute biological and mineral extracts administered IA for painful knee OA. In response to clinician impressions of positive outcomes, a db-RCT to assess efficacy and safety compared to IA saline was deployed in the US.

Methods:
Pts with moderate-to-severe chronic knee OA were randomized to 3 weekly IA injections of either Tr14 & Ze14 or saline by clinical investigators experienced with use of the IA injection route. The primary efficacy variable was change in knee pain from Baseline to End-of-Study (Week 17) as measured by the WOMAC OA Pain Subscale (Section A, 1-5) 100 mm VAS. Secondary measures included Total WOMAC and subscores for stiffness (B), and physical function (C), change in pain following a 50 ft walk (100 mm VAS), patient and physician global assessments. Clinical relevance was assessed by comparing proportions of patients with reductions from baseline in WOMAC A scores greater than a validated benchmark Minimal Clinically Important Difference (MCID). This was chosen as -32.6 mm (the most conservative value) based on a study of outpatients with knee or hip OA where WOMAC VAS MCIDs ranged from -7.9mm to -32.6mm [see reference 59 Tauback et al., *Ann Rheum Dis.* 2005; 64(1):29-33 in the description of the WOMAC index published by ACR]. Safety was assessed by monitoring of vital signs, physical examinations of the target knee, adverse events and concomitant medications.

Results:
232 patients were randomized and treated (All Tr14 & Ze14, n=119, All Placebo, n=113; Intention-to-Treat (ITT) Tr14 & Ze14, n=117, Placebo, n= 111). Treatment arms were well balanced across demographic and baseline characteristics. Tr14 & Ze14 did not discriminate for WOMAC A Pain as expected after only 1 of 3 injections on Day 8 ($p=0.3715$), but subsequently was significantly different ($p<0.05$) on Days 15, 43, 57, 71, 85 and 99 (primary endpoint day), and approached significance on Day 29 ($p=0.0686$). Logistic regressions showed the proportion of MCID responders was not significant on Day 8. As this was an expected finding, it served as a no-effect internal-model-validation. Tr14 & Ze14 was significantly different ($p<0.05$) on all subsequent days except Day 29 (approached significance, $p=0.0599$, Figure 1). 50' walk pain was similarly discriminating as was the physician global assessment. Total WOMAC and subscores B&C were directionally consistent with WOMAC A. There were no related SAEs. AEs were generally mild and unrelated to treatment. Local knee-related AEs, lab assessments, ECGs and vital signs were unremarkable and similar between treatments.

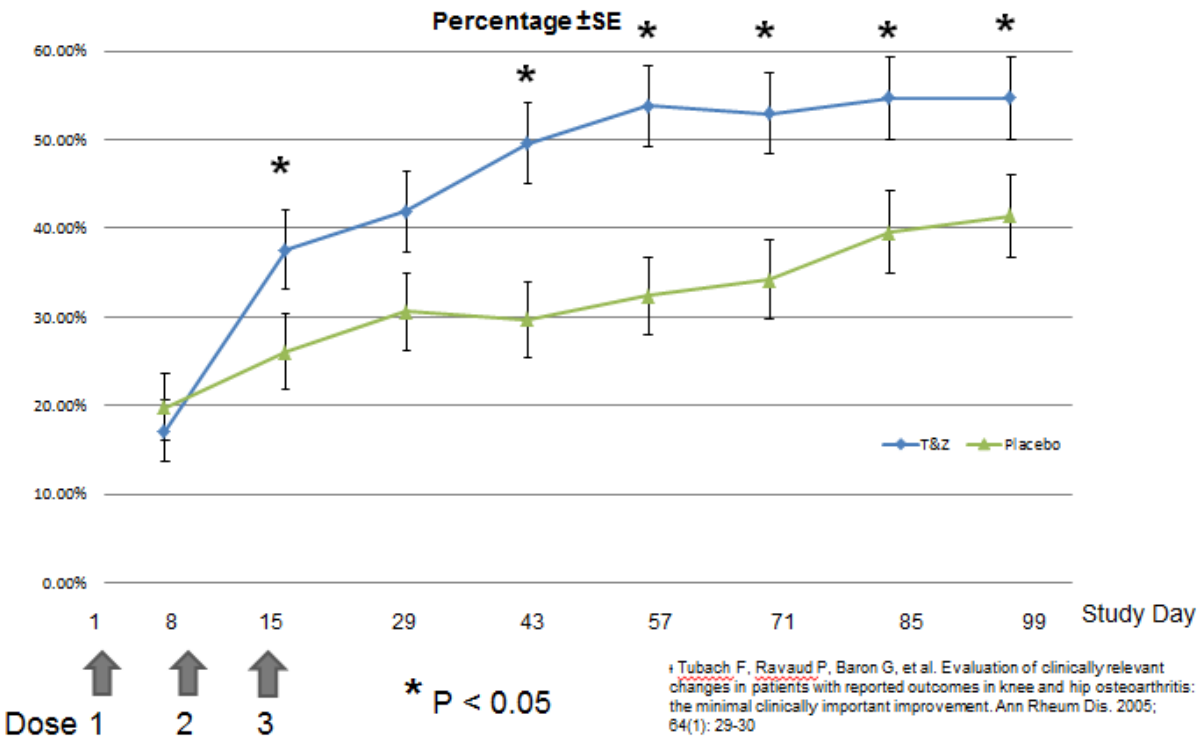

Figure: Proportion of patients meeting validated criterion for response on WOMAC Subscale A; ITT population with LOCF; Minimally Important Difference (MID) from baseline = -32.6mm.

Conclusion:
Tr14 & Ze14 provided statistically significant and clinically relevant pain relief on days 15 to 99 in comparison to placebo. In this double-blind, randomized, controlled trial, a biological/mineral multi-extract combination was shown to be a safe and effective treatment for pain in moderate-to-severe knee OA.

Disclaimer:
These statements have not been reviewed by the Food and Drug Administration. They are supported by traditional homeopathic principles.