evolutionary course, the loss of BMI only showed a tendency to correlate with the decrease in bone mass in the femoral neck (p -value 0.089), but not in the other locations.

Conclusion: In our sample of morbidly obese patients undergoing bariatric surgery, there is a significant and widespread loss of bone mineral density one year after the procedure, all this despite the supplementation and the increase in 25OHD levels. This loss only seems to be directly related to the decrease in weight at the femoral neck, just probably by a mechanism to reduce mechanical load.

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Osteoarthritis

FRI0378

GENERAL SAFETY AND TOLERABILITY OF SUBCUTANEOUS TANEZUMAB FOR THE TREATMENT OF OSTEOARTHRITIS: A POOLED ANALYSIS OF RANDOMIZED, PLACEBO-CONTROLLED TRIALS

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Background: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for the treatment of signs and symptoms of osteoarthritis (OA).

Objectives: To assess the safety and tolerability of subcutaneous (SC) tanezumab in patients with OA.

Methods: Data were derived from 3 randomized placebo-controlled OA trials. SC treatment (every 8 weeks for 16–24 weeks with 8–24 week follow-up) included placebo, tanezumab 2.5mg, tanezumab 2.5/5mg (2.5mg at day 1 and 5mg at week 8), and tanezumab 5mg. Overall treatment-emergent adverse events (TEAEs) and TEAEs of abnormal peripheral sensation were pooled from all 3 trials (placebo N = 586; tanezumab: 2.5mg N = 602, 2.5/5mg N = 219, 5mg N = 347). Pre-specified TEAEs potentially associated with sympathetic neuropathy (anhidrosis, bradycardia, hypohidrosis, orthostatic hypotension, or syncope) and pre-specified joint events (primary osteonecrosis, rapidly progressive OA [RPOA] type 1 or type 2, subchondral insufficiency fracture, or pathological fracture; adjudicated by an independent committee of experts) were pooled from the 2 trials that included prospective evaluation of sympathetic and joint safety (placebo N = 514; tanezumab: 2.5mg N = 528, 2.5/5mg N = 219, 5mg N = 284). TEAEs are presented for the treatment period; joint safety is presented for the full study (treatment plus follow up) period.

Results: Patient demographics (80.7% white, 66.8% female, mean age $\approx$ 63 years) and clinical characteristics were similar across groups. TEAE rates were: placebo = 51.7%, tanezumab 2.5mg = 52.3%, tanezumab 2.5/5mg = 47.0%, and tanezumab 5mg = 54.8%. Of TEAEs occurring in $\geq 2\%$ of patients in any group, only oedema peripheral, joint stiffness, and paraesthesia had a higher incidence (95% confidence interval excluded 0) in any tanezumab group relative to placebo. Serious TEAE rates were: placebo = 1.5%, tanezumab 2.5mg = 2.2%, tanezumab 2.5/5mg = 1.4%, and tanezumab 5mg = 2.6%. Rates of treatment and/or study discontinuation due to TEAEs were: placebo = 2.2%, tanezumab 2.5mg = 1.8%, tanezumab 2.5/5mg = 0.5%, and tanezumab 5mg = 1.4%. Only arthralgia and OA led to discontinuation in >1 patient in any group. TEAEs of abnormal peripheral sensation rates were: placebo = 2.2%, tanezumab 2.5mg = 5.1%, tanezumab 2.5/5mg = 3.2%, and tanezumab 5mg = 6.1%. Paraesthesia and hypoaesthesia were the most common events. Potential sympathetic neuropathy TEAE rates were: placebo = 0.8%, tanezumab 2.5mg = 1.5%, tanezumab 2.5/5mg = 0.5%, and tanezumab 5mg = 2.8%; exposure-adjusted rates were not statistically different between any tanezumab group and placebo. Bradycardia and orthostatic hypotension were the most common events. No patient was considered to have a sympathetic neuropathy. TEAEs of abnormal peripheral sensation and potential sympathetic neuropathy were mostly mild and resolved. Joint safety event rates

were statistically different for tanezumab 5mg (3.2%), but not 2.5mg (1.9%) or 2.5/5mg (0.5%), compared to placebo (0%). RPOA type-1 was the most common event. Total joint replacement rates were: placebo = 4.5%, tanezumab 2.5mg = 5.9%, tanezumab 2.5/5mg = 6.8%, and tanezumab 5mg = 7.0%; rates were not statistically different between any tanezumab group and placebo.

Conclusion: Tanezumab was generally safe and well tolerated in most patients, with rates of overall TEAEs and treatment/study discontinuations similar to placebo and no evidence of a sympathetic safety signal. TEAEs of abnormal peripheral sensation and joint safety events were infrequent but more common with tanezumab than placebo.

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VARIATIONS IN THE UTILIZATION OF BILATERAL TOTAL KNEE ARTHROPLASTY IN THE MANAGEMENT OF OSTEOARTHRITIS

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Background: A third of knee osteoarthritis presents with bilateral symptomatic arthritis. In these patients, treatment options include either a staged Unilateral Total knee arthroplasty (UTKA) procedure, or a simultaneous Bilateral TKA (BTKA) procedure. Even though literature regarding outcomes in BTKA procedure has not consistently been favorable, it remains popular in select patients due to use of a single anesthetic, shorter overall surgical time, lower cost and lower overall use of narcotics. African Americans (AAs) have lower utilization and worse outcomes in UTKA literature. It is unclear whether these racial variations extend to BTKA.

Objectives: We sought to examine BTKA vs UTKA utilization rates and outcomes comparing AA and White patients.

Methods: National Inpatient Sample (NIS) - Healthcare Cost and Utilization Project (HCUP) database (2007-2016) was used. We identified all patients $\geq$ 50 years who underwent elective primary TKA using ICD-9-CM code 81.54 for UTKA and BTKA from January 1, 2012 to September 30, 2015, and ICD-10-CM codes 0SR00x and 0SRD0x thereafter. Patients with inflammatory arthritis, pathologic fractures, metastatic disease and avascular necrosis were excluded. Major in-hospital complications included post-operative myocardial infarction, prosthetic device complication, surgical wound infection, and venous thromboembolism. Differences in temporal trends in utilization and major in-hospital complications of BTKA vs UTKA were compared between AAs and Whites. Multivariable logistic regression models were used to assess differences in both these trends between AAs and Whites after adjusting for individual (age, sex, Elixhauser comorbidity index, and morbid obesity), hospital level (hospital volume, bed size, region and teaching status) and community level (median household income) variables. Discharge weights were used to enable nationwide estimates. Multiple imputation was performed for missing race variable (11.9%).

Results: From 2007 to 2016, an estimated 276,194 BTKA (unweighted observations 56,675) and 5,528,429 UTKA (unweighted observations 1,131,329) were identified (Table 1). Females had a higher proportion of TKAs performed (62.1% UTKA vs 55.9% BTKA). Patients had fewer comorbidities (measured by the Elixhauser Index) when undergoing BTKA compared to UTKA. The proportion of BTKA amongst all TKAs declined from 5.53% in 2007-08 to 4.03% in 2015-16. AAs continued to have significantly lower proportion of BTKA utilization compared to Whites (4.68% in AAs vs 6.08% in Whites in 2007-08, whereas 3.28% in AAs vs 4.19% in Whites in 2015-16, adjusted $p < 0.001$) (Figure 1a). In-hospital complication rates for UTKA and BTKA were significantly higher in Whites compared to AAs throughout the study period (0.77% in AAs vs 0.9% in Whites in 2007-08, whereas 0.69% in AAs vs 0.83% in Whites in 2015-16,

adjusted $p < 0.001$) (Figure 1b). The results were similar after imputation of missing race values.

Conclusion: In this nationwide sample of patients from 2007 to 2016, we found that AAs have lower utilization rate of BTKA compared to Whites, however the in-hospital complication rates were significantly higher in Whites.

References: N/A

Table 1. Weighted frequencies and percentages of demographic characteristics among unilateral TKA vs. bilateral TKA (N = 6, 236, 426).

Variable	Unilateral TKA N = 5,528,429 (Unweighted N = 1,131,329)	Bilateral TKA N = 276,194 (Unweighted N = 56,675)	P ^a
Patient Characteristics			
Age, mean (SD)	67.4 (0.02)	65.0 (0.06)	<.0001
Sex: Female, n(%)	3,429,484 (62.1)	154,442 (55.9)	<.0001
Race, n(%)			
White	4,051,648 (50.9)	212,468 (76.9)	<.0001
African American	352,933 (6.4)	14,441 (5.2)	
Other	464,407 (8.4)	16,443 (6.0)	
Missing	659,439 (11.9)	32,842 (11.9)	
Morbid Obesity, n(%)	401,892 (7.3)	20,411 (7.4)	0.47
Elixhauser Index ^d , n(%)			<.0001
0	716,559 (13.0)	41,550 (15.0)	
1-4	4,484,941 (81.1)	220,638 (80.0)	
≥ 5	326,928 (5.9)	14,007 (5.1)	

Figure 1a: Difference in trends in Utilization of BTKA vs UTKA between Whites and African Americans (AAs).

Note: Percentage of bilateral TKAs is defined as the number of bilateral TKAs among total TKAs in each period

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Figure 1b: Trends in in-hospital complications of BTKA vs UTKA between Whites and African American (AAs).

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ITEMS DRIVING WOMAC PAIN SUBSCORE CHANGES DUE TO LORECEVIVINT, A POTENTIAL DISEASE-MODIFYING TREATMENT FOR KNEE OSTEOARTHRITIS: A POST HOC ANALYSIS OF PHASE 2B TRIAL DATA

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Background: Knee osteoarthritis (OA) is a disease characterized by pain, loss of function, and structural deformities, leading to a heterogeneous disease state that can confound patient-reported outcomes (PROs). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain subscore addresses this reporting variability by capturing multiple pain items related to 'active' and 'static' subject states. We hypothesize that measurement of these 'active' versus 'static' pain items may demonstrate differential effect sizes when assessing treatment benefit. Lorecivint (LOR; SM04690), a small-molecule, intra-articular CLK/DYRK1A inhibitor that modulates the Wnt pathway, is currently in development as a potential disease-modifying treatment for knee OA.^{1,2}

Objectives: To test the hypothesis, a post hoc analysis of Pain NRS, the WOMAC Pain subscore, and individual WOMAC PROs (items A1–A5) from a Phase 2b LOR trial was performed to examine effect size (ES) changes.

Methods: The original 24-week Phase 2b trial has been previously reported. In this study, pain was assessed using the weekly average of daily Pain NRS and WOMAC Pain subscore. In the post hoc analysis, items A1–A5 (pain walking on a flat surface? [A1], going up/downstairs? [A2], at night in bed? [A3], sitting or lying down? [A4], and while standing? [A5]) were individually analyzed for subjects treated with 0.07 mg LOR and compared with the primary study outcomes of mean Pain NRS and summed mean WOMAC Pain subscore at Week 12. Baseline-adjusted analysis of covariance for WOMAC A1–A5 scores was conducted on LOR-treated subjects compared with placebo (PBO) in 1) the Full Analysis Set (FAS) of all dosed subjects and 2) a target population of subjects with fixed baseline joint space width (JSW) [2–4] mm without widespread pain (Widespread Pain Index [WPI] ≤4, Symptom Severity Score Question 2 ≤2).

Results: In this analysis, 231 subjects (KL grade 3 63.2%) were included. The primary study analysis demonstrated efficacy of LOR compared with PBO for Pain NRS and WOMAC Pain, with respective effect sizes of 0.450 and 0.293 (Figure). In the target population, Pain NRS and WOMAC A effect sizes increased (0.637 and 0.410, respectively). Each WOMAC A item showed less of an effect size than Pain NRS at Week 12. Treatment with 0.07 mg LOR compared with PBO showed significant improvements in effect sizes of WOMAC A1 (FAS: ES=0.315, $P=0.028$; target population: ES=0.421, $P=0.035$) and A2 (FAS: ES=0.392, $P=0.006$; target population: ES=0.510, $P=0.011$). A3–A5 did not show statistical improvement for LOR compared with PBO.

Figure. Effect sizes for 0.07 mg LOR compared with PBO for the FAS and target population at Week 12.

Conclusion: In the post hoc analysis, Pain NRS exhibited the greatest effect size of tested PROs after treatment with 0.07 mg LOR compared with PBO. These effect sizes were enhanced in the target population with fixed baseline JSW and without widespread pain for all scores relative to the FAS. WOMAC 'active' questions demonstrated greater effect sizes with LOR treatment than 'static' questions and the full WOMAC Pain domain, providing support for the hypothesized dimensional constructs in knee OA pain assessment.