THU0441

IMPROVED KNEE PHYSICAL FUNCTION CORRELATES SIGNIFICANTLY WITH TIBIOFEMORAL CARTILAGE THICKNESS INCREASE AFTER IA TPX-100: RESULTS OF A POST HOC ANALYSIS

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Background: In new draft guidance for OA drugs, the U.S. FDA notes the "well-recognized discordance" in clinical trials between structural imaging and patient benefit. In a randomized, double-blind, placebo-controlled trial, IA TPX-100 was associated with statistically significant and clinically meaningful improvement in knee functions among subjects (n=93) recruited for mild-moderate (ICRS grades 2-3) bilateral patellofemoral OA. No treatment differences in PF cartilage were detected, consistent with FDA concerns. However, only 14% of knees had measurable PF cartilage change on follow-up MRIs, limiting power for analysis of treatment differences in PF cartilage (ACR/ACHP 2017).

Objectives: To conduct a subset analysis of knee function and cartilage thickness correlations among the 73% of subjects (n=68) who had, in addition to PFOA, bilateral tibiofemoral OA (TFOA).

Methods: Subjects received 4 weekly injections of IA TPX-100 in one knee and identical saline placebo in the contralateral knee, as randomly assigned. MRIs were obtained at baseline, 6 and 12 months; and patient-reported outcomes (KOOS/WOMAC) were obtained at baseline, 3, 6 and 12 months. Subjects, sites, sponsor and central readers were blind to treatment assignment. All subjects receiving 4 weekly injections of 200 mg TPX-100 with at least one follow-up MRI were included for efficacy. The database was locked prior to all analyses, and clinically meaningful differences in outcome measures were selected *a priori*, based on the literature (Roos 2003).

Results: Of 68 subjects with bilateral TFOA, 47% had ICRS grade 4 (severe) TFOA at baseline, and 43% had ICRS grade 3 (moderate) disease. Demographics for this cohort were consistent with the U.S. knee OA population in mean age (60.8 years), BMI (30.6), and gender distribution (60% females). IA TPX-100 was safe and well tolerated, with no drug-related serious adverse events or safety concerns. The mean functional improvement of TPX-100-treated knees was significantly higher than that of placebo-exposed knees at 6 and 12 months ($p < 0.04$ and $p < 0.02$, respectively). Responder knees, defined *a priori* with ≥ 8 points increase in KOOS physical function, had mean improvements in function of 20.5 and 22.4 at 6 and 12 months, respectively. Pearson analysis revealed a significant positive 12-month correlation ($p < 0.05$) between degree of functional improvement and cartilage thickness increase/stabilization in TF cartilage in TPX-100-treated knees (Table 1).

Abstract THU0441 –Table 1.

Cartilage Thickness vs. Knee Function (KOOS ADL)

Month	Cartilage Thickness	Pearson Correlation	
12	Correlation	p-value	
	Lateral TF	0.359	0.003
	Medial TF	0.242	0.048
	Entire TF	0.332	0.007

Conclusion: In subjects with bilateral TFOA, statistically significant and clinically meaningful, robust functional improvements in TPX-100-treated knees were seen at 6 and 12 months compared with placebo-exposed knees. Formal analysis revealed statistically significant correlations between functional improvement and increase or stabilization of lateral, medial and total TF cartilage thickness. To our knowledge, TPX-100 is the first candidate DMOAD to show improvement in critical knee function concordant with increase/stabilization of cartilage structure compared with placebo-exposed knees.

REFERENCE:

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THU0442

SOCIAL VULNERABILITY AND DISCHARGE DISPOSITION AFTER ELECTIVE TOTAL HIP REPLACEMENT? RISK-ADJUSTED ANALYSIS OF LARGE REGIONAL DATASET

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Background: With the aging of the world population and the rising prevalence of Osteoarthritis (OA), elective joint replacement (JR) has become one of the fastest growing procedures in the management of end-stage OA. There is also increasing evidence that social determinants of health such as where one lives impact healthcare utilization and decision-making. Furthermore, elective JR of the hip and knee is one of the most important cost-centers for Medicare, the largest payer in the US, and has therefore been the subject of ongoing payment reform models that shape discharge destination and risk of readmission.

Objectives: In a large regional dataset, we sought to examine how social vulnerability impacts discharge destination after elective THR, and what is the role in this relationship of patient race, another key social determinant of health which has been previously associated with disposition after surgery.

Methods: We used the Pennsylvania Health Care Cost Containment Council (PHC4) database to identify all patients who underwent elective THR between 2012 and 2016. Community level Social Vulnerability Index (SVI) was derived from the American Census Survey, which draws 15 different measures of vulnerability including socioeconomic, housing, and disability among others. SVI ranges from 0 (least vulnerable) to 1 (most vulnerable). SVI was dichotomized into low (below median) and high (above median). We used binary logistic regression to test the association between community SVI and discharge disposition: Institution (Nursing home or inpatient rehabilitation vs Home with/out home health). We adjusted for important clinical, demographic, and facility level covariates. To examine the role race (African American (AA) vs White) in this relationship, we included in the model an interaction term for SVI and race.

Results: There were a total 86,215 THR done between Jan 2012 and Dec 2016 that met our inclusion criteria. About 40,881 were <65 years of age; and 45,334 were ≥ 65 years of age. Patients from low SVI community went to high volume hospitals as compared to high SVI in all age groups. Figure 1 shows the geospatial localization and relationship of THR patients in the State of Pennsylvania by community SVI level. Compared to white patients, AA patients were more likely to live in higher SVI communities (median SVI_{AA} 0.66; IQR 0.48-0.83 vs median SVI_W 0.42; IQR 0.28-0.55, respectively). Compared to low SVI communities, patients from high SVI communities were more likely to be discharged to an institution (vs home) (for age <65; aOR= 1.22, 95% CI: 1.14,1.30, $p < 0.001$; for ages ≥ 65 ; aOR= 1.11,95% CI: 1.07,1.16, $p < 0.001$). The odds of discharge to an institution (vs Home) for patients living in high SVI communities (vs low SVI) was higher in AA compared to whites in all age groups. [Figure 2].

Conclusion: In this large regional dataset of patients who underwent THR, social vulnerability index of the community is associated with discharge disposition after surgery. Moreover, this association was stronger in African-Americans compared to Whites. This association when coupled with ongoing payment reform models may have implications for access to care for socially vulnerable populations.