Background: In new draft guidance for OA drugs, the U.S. FDA notes America” that "there was significant positive 12-month correlation (p<0.05) between degree of function improvement and cartilage thickness increase/stabilization in TF cartilage among the 73% of subjects (n=68) who had, in a priori planned analysis, a statistically significant and clinically meaningful improvement in knee function 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/ACP 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 knee and identical saline placebo in the contralateral knee, as randomly assigned. MRIs were obtained at baseline, 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. Demographic data and clinical characteristics were consistent with the U.S. 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 in 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.

<table>
<thead>
<tr>
<th>Month</th>
<th>Cartilage Thickness</th>
<th>Pearson Correlation</th>
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<tbody>
<tr>
<td></td>
<td>Correlation</td>
<td>p-value</td>
</tr>
<tr>
<td>12</td>
<td>Lateral TF</td>
<td>0.359</td>
</tr>
</tbody>
</table>

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 concomitant with increase/stabilization of cartilage structure compared with placebo-exposed knees.

REFERENCE:
and total scale were normalized to 0-100 scales. The participants also completed the Numeric Rating Scale (NRS, 0-10 scale) about hand pain, the Canadian (AUSCAN) hand pain subscale (0-20 scale) and questionnaires about psychological factors; Hospital Depression and Anxiety Scale (HADS, 0-42 scale), Pain Catastrophizing Scale (PCS, 0-52 scale) and the pain subscale of the Arthritis Self Efficacy Scale (ASES, 10-100 scale). For all scales except ASES, high scores indicate poor health. We identified the adjectives in the McGill questionnaire with most frequent responses. To determine the external validity, the McGill questionnaire was correlated to other questionnaires (AUSCAN, NRS, HADS, PCS and ASES) using Spearman correlation coefficients.

Results: The participants (89% women) with median (IQR) age of 61 (57-66) years demonstrated a wide range in pain characteristics and intensity, with a median (IQR) of 34.5 (0-62.3), 14.9 (0-39.2) and 44.2 (34.9-48.8) for the sensory, affective and evaluate subscales, respectively. The median for the total pain sum score was 29.7 (7.0-53.2). A floor effect was detected for the sensory (23.7% with score 0) and affective (40.3% with score 0) subscales. The reported adjectives with highest frequency were “sore” (n=208, 69.3%), “inhibiting” (n=124, 41.3%) and “annoying” (n=97, 32.3%). The participants frequently reported neuropathic-like characteristics such as sticking/stabbing/pricking (n=137, 45.7%), speeding/radiant (n=110, 36.6%), smarting/burning (n=89, 29.6%) and creeping (n=43, 14.3%).

The McGill total scale showed moderate correlations with AUSCAN and NRS pain (Table). Similar strength of correlations was found for all the subscales, and stronger for the intensity score (0.63-0.64). The correlation with HADS was similar for the McGill questionnaire, AUSCAN and NRS pain. The correlations with PCS and ASES were weaker for McGill than for the other pain questionnaires.

Conclusion: The McGill Pain questionnaire may be a useful tool in research settings for a broad evaluation of pain characteristics in hand OA. Moderate correlations with other pain questionnaires suggest that the McGill questionnaire measures other constructs. For the first time, we have shown that neuropathic-like pain characteristics are frequently reported by persons with hand OA.