Cartilage damage in both the index knee and non-index knee (without IA injection) were evaluated in MRI images taken at study sites by dedicated local radiologists using the semiquantitative MRI Osteoarthritis Knee Score (MOAKS) instrument, which indicated the progression of knee joint cartilage deterioration:

a) The knee joint was divided into 14 sub-regions for grading (Figure 2).

RESULTS & DISCUSSION

In the TLC599A2003 study, subjects treated with TLC599 12mg displayed a significantly greater reduction in pain than placebo throughout all specified time points, especially in Weeks 11, 16, 20, and 24 (p < 0.05). This demonstrated the sustained duration of pain control by TLC599 for at least 6 months.

During the 24 weeks study period, both the changes in surface area loss and full thickness loss were also evaluated in subjects’ knees. MOAKS sub-region scores were compared between placebo, which represents the natural course of the disease knees, and the TLC599-treated patient knees were assessed. Index knees were compared with the non-index knees for the subject distribution in 2 levels of worsening (worsening in MOAKS score ≤ 1 vs. worsening in MOAKS score ≥ 2; MOAKS ≥ 2 representing significant worsening) over 24 weeks period, regardless of the individual sub-region severity (Table 1).

The exploratory MRI evaluation of knee cartilage using semi-quantitative MOAKS indicated that, comparing index to non-index knees, patients treated with TLC599 IA injection displayed less cartilage loss in the treated knee than placebo patients, suggesting a lack of cartilage damage or potentially a chondroprotective effect.

CONCLUSION

The exploratory MRI evaluation of knee cartilage using semi-quantitative MOAKS indicated that, comparing index to non-index knees, patients treated with TLC599 IA injection displayed less cartilage loss in the treated knee than placebo patients, suggesting a lack of cartilage damage or potentially a chondroprotective effect.

ACKNOWLEDGEMENT

The authors wish to acknowledge the efforts of all the clinicians and studies participating in the TLC599A2003 study, particularly Dr. Graham Roulstone on behalf of the use of MOAKS for assessing cartilage damage with MRI.

Table 2. Difference in proportions with cartilage deterioration between index knee and non-index knee

The absence of central imaging reading and the small sample size prevented the direct statistical evaluation of cartilage damage between TLC-treated and placebo-subjects with statistical analysis.

REFERENCES


The pattern of knee joint cartilage damage change between treated groups was reflected by the difference between the proportions of subjects displaying ≥ 2 cartilage sub-regions in index/non-index knees (Table 2).

Table 1. Comparison of significant cartilage loss between TLC599-and placebo-treated patients

For the placebo group, the index knee displayed similar or more significant cartilage damage than the non-index knee: 5% (index knee) vs 5% (non-index knee), and 4% (index knee) vs 5% (non-index knee) of patients showing ≥ 2 worsening in sub-region surface area loss and full thickness loss, respectively. However, TLC599-treated patients displayed lower proportions of significant cartilage damage in the index knee than the non-index knee. For the TLC599 12mg cohort, there were 42% (index knee) vs 50% (non-index knee), and 29% (index knee) vs 33% (non-index knee) of patients showing ≥ 2 worsening in sub-region surface area loss and full thickness loss, respectively. A similar trend was seen in the TLC599 18mg cohort. These findings suggest there may be protection from or delay in cartilage degeneration by TLC599 injection in patients with knee OA.

CONCLUSION

The exploratory MRI evaluation of knee cartilage using semi-quantitative MOAKS indicated that, comparing index to non-index knees, patients treated with TLC599 IA injection displayed less cartilage loss in the treated knee than placebo patients, suggesting a lack of cartilage damage or potentially a chondroprotective effect.

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