

Fatty Acid Binding Protein 5 Inhibitor ART26.12 Provides Immediate and Lasting Analgesia for Osteoarthritic Pain

Adam J. Bruzzese¹, Kai L. Bou², Kaitlin M. Farrell¹, Chris Gordon¹, Martin Kaczocha², David E. Komatsu¹

¹Department of Orthopaedics and Rehabilitation, Renaissance School of Medicine, Stony Brook University, Stony Brook, NY, USA

²Department of Anesthesiology, Renaissance School of Medicine, Stony Brook University, Stony Brook, NY, USA

adam.bruzzese@stonybrookmedicine.edu or kai.bou@stonybrook.edu

Disclosures: This study was supported by Artelo Biosciences, Inc. M.K. has patents issued to the Research Foundation of the State University of New York.



INTRODUCTION

- Chronic pain associated with knee osteoarthritis (OA) lacks safe, efficacious long-term analgesic treatments due to the complexity of pain signaling pathways.
- Non-steroidal anti-inflammatory drugs (NSAIDs) have short-term efficacy but suffer gastrointestinal risks.
- Fatty-acid binding protein 5 (FABP5) inhibition has been shown to exhibit analgesic activity by modulating fatty acid transfer within the endocannabinoid system (ECS).
- ART26.12 demonstrates selective binding to FABP5, antinociceptive properties, less off-target liabilities, and increased oral bioavailability
- Aim: Investigate efficacy of FABP5 inhibition in reducing OA pain using the novel drug, ART26.12, in a rat model.

METHODS

- Experiments were approved by the Stony Brook University Institutional Animal Care and Use Committee (#277150).
- 50 Female Sprague Dawley rats underwent surgical destabilization of the medial meniscus (DMM). Eight weeks post-surgery, five rat groups (N=10) received acute dosing (PO BID) of vehicle, 8 mg/kg naproxen, and three concentrations of ART26.12 (10, 25, and 50 mg/kg).
- Static incapacitance (reported as an averaged ratio of ipsilateral to contralateral hindlimb weight bearing) and grip strength (averaged ratio of ipsilateral force (g) to rat weight (g)) were measured at 1 and 4 hours after acute dosing (Fig. 1), and weekly from weeks 8-12 post-DMM during the chronic dosing phase (same dosing regime) (Fig. 2).
- Results are presented as dot plots with mean and 95% confidence intervals overlaid; normality was confirmed with Shapiro-Wilk tests (Fig. 1-4).
- Comparisons within each dosing group were made using one-way repeated measures ANOVA followed by Dunnett's multiple comparisons with the baseline data as the control group. Significance (Fig. 1,2,4) was defined with the following p-values:
 - * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$; **** = $p < 0.0001$
- All analyses were performed using Prism (Ver. 10.4.1, GraphPad).

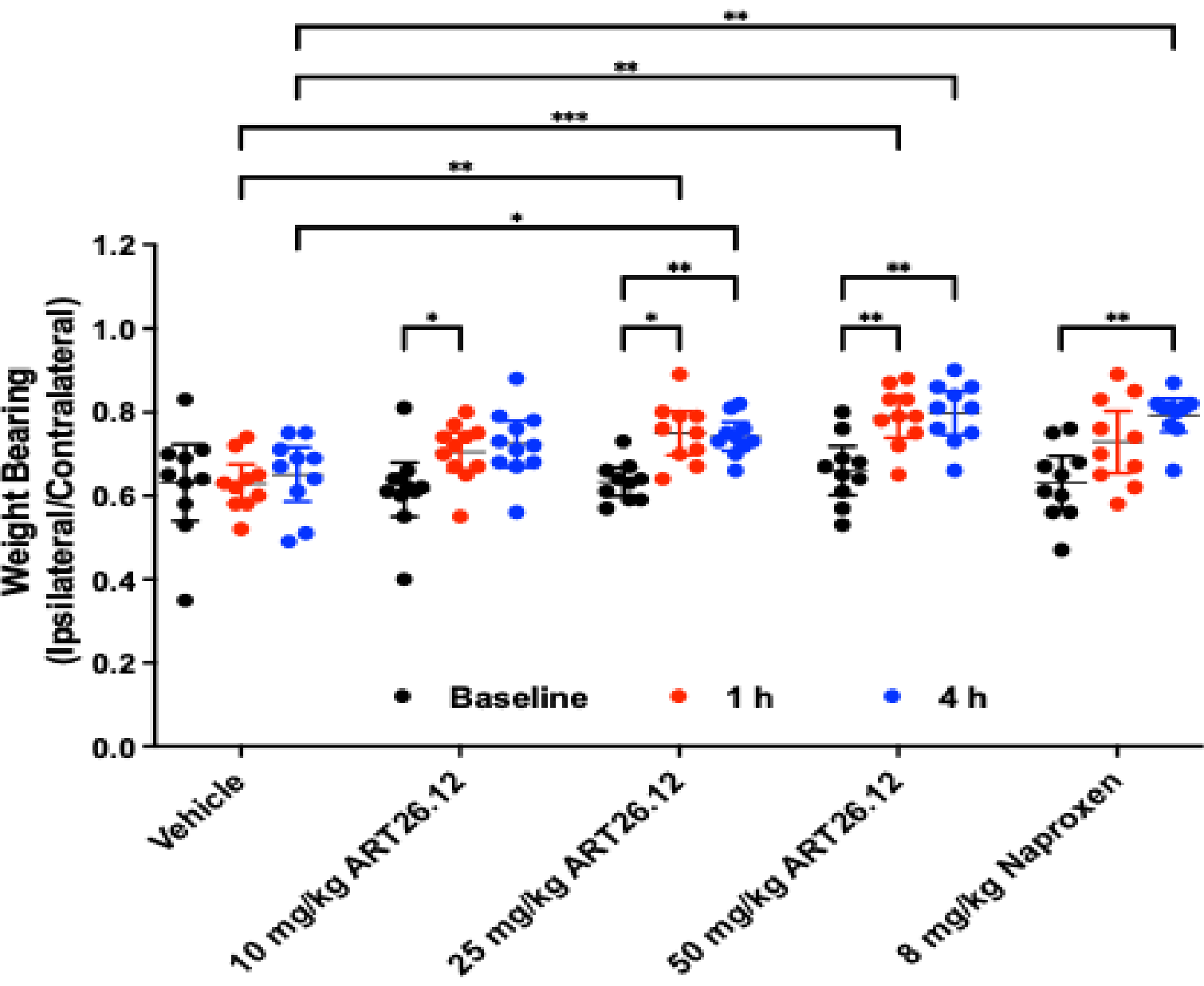


Figure 1. Acute Incapacitance

Acute ART26.12 dosing reduced weight-bearing asymmetry compared with vehicle, indicating improved pain-related behavior

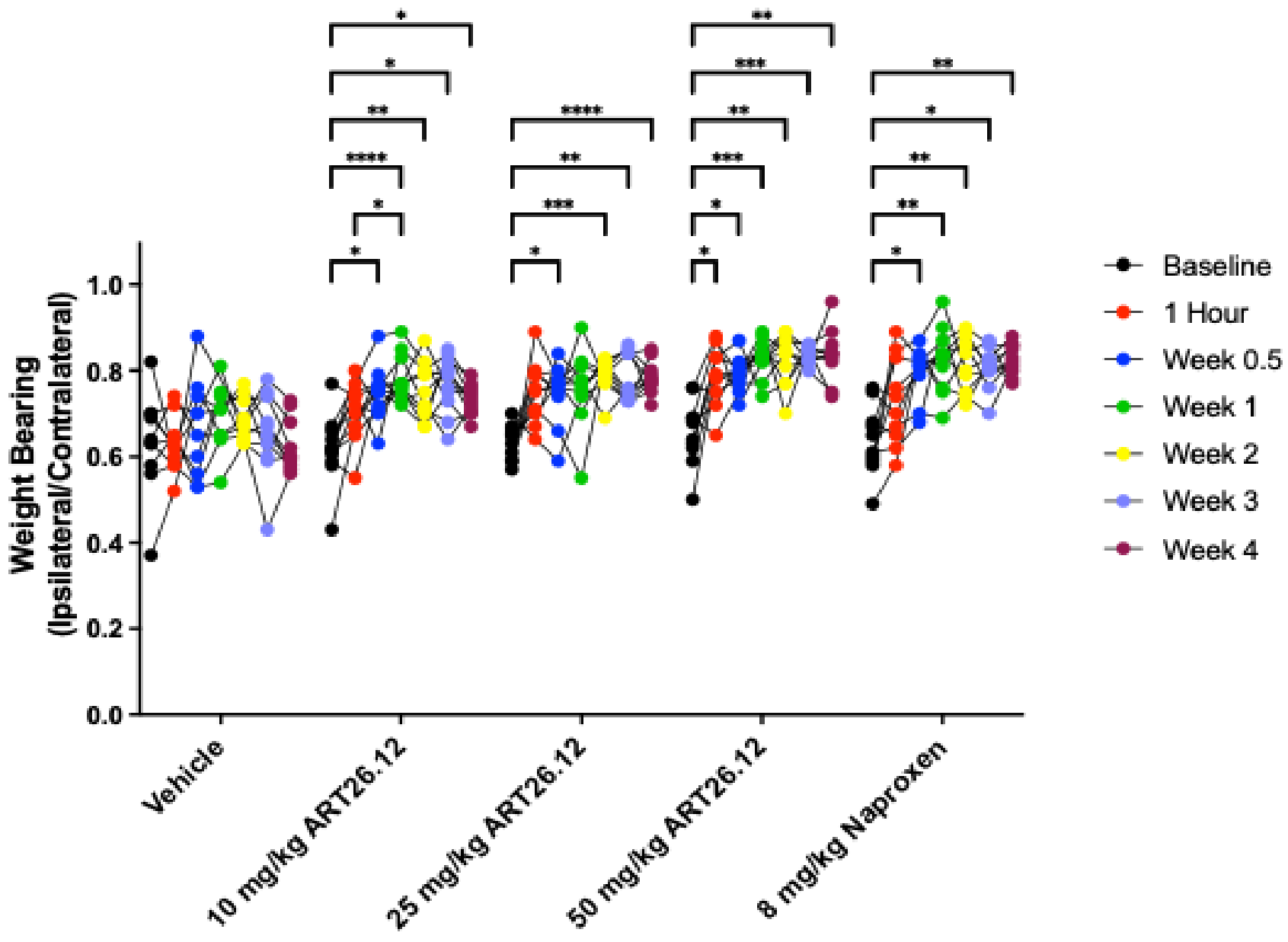


Figure 2. Chronic Incapacitance

Chronic ART26.12 treatment produced sustained improvement in incapacitance over time relative to vehicle.

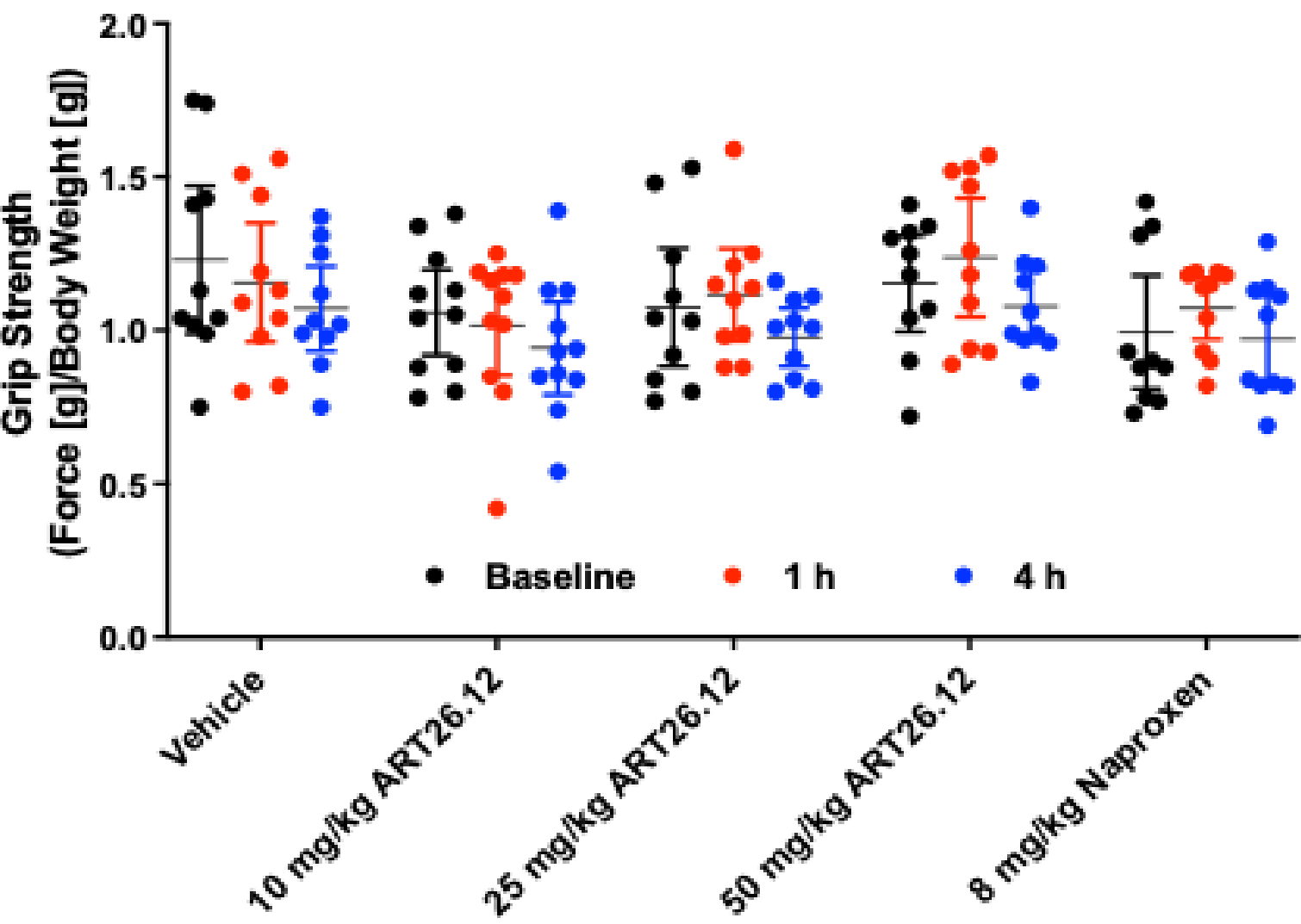


Figure 3. Acute Grip Strength

Acute dosing showed limited change in grip strength, suggesting lower sensitivity of this measure for knee pain.

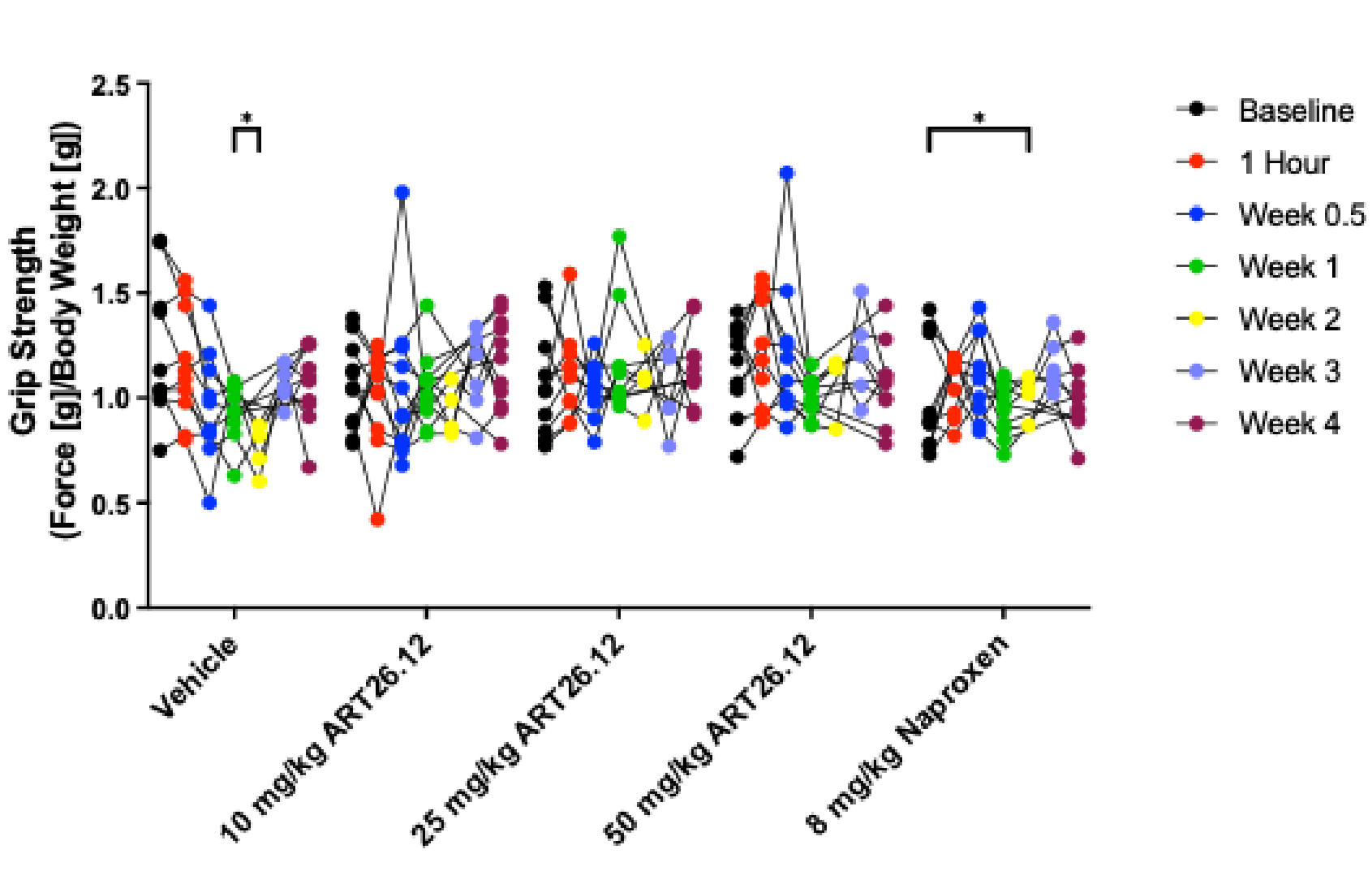


Figure 4. Chronic Grip Strength

Chronic treatment did not significantly improve grip strength despite benefit seen in incapacitance testing.

RESULTS

- Expectedly, the vehicle group exhibited no differences in incapacitance with acute or chronic dosing (Fig. 1,2).
- In acute dosing, the ART26.12 groups demonstrated significantly increased weight bearing on the ipsilateral (arthritic) limb versus the contralateral limb, indicated by increased weight bearing ipsilateral/contralateral ratios between baseline and post-dose timepoints (Fig. 1).
- With higher ART26.12 concentrations, from 10 mg/kg to 25 mg/kg and 50 mg/kg, there was a more pronounced, statistically significant increase in ipsilateral weight bearing from baseline to 1-hour and 4-hour post-dose timepoints.
- In acute dosing, the 8 mg/kg naproxen group showed a significant increase in ipsilateral weight bearing only at the 4-hour post-dose time point (Fig. 1).
- In chronic dosing, there were significant increases in ipsilateral weight bearing between weeks 0.5-4 for ART26.12 treatment groups, with similar increases observed in the naproxen group (Figure 2). No significant differences were observed in acute or chronic grip strength measurements across groups or timepoints (Figure 3,4).

DISCUSSION

- Increased weight bearing ratios across all timepoints suggest that ART26.12 reduced OA-induced pain acutely and chronically, with chronic incapacitance data demonstrating that ART26.12 effectiveness did not decrease with time.
- Despite similar effectiveness of naproxen and ART26.12 in chronic incapacitance, ART26.12 may still be more favorable than NSAIDs if histological analysis reveals healthier gastrointestinal tracts in ART26.12 groups.

LIMITATIONS

- Modest sample sizes may have limited power to detect smaller differences, especially for grip strength outcomes.
- Absent significant grip strength variation may be due to minimal isolated pressure to the knee during grip action.
- Use of only female rats in a single DMM osteoarthritis model limits generalizability to males and human OA.
- Pain assessment relied on behavioral surrogate measures without histologic, mechanistic, or long-term safety data.

