Preliminary Efficacy Data Of Grapiprant, Bedinvetmab And Negative Control In Dogs With Experimentally Induced Synovitis

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Objective

Investigation of the efficacy of oral grapiprant compared to injectable bedinvetmab and a negative control in an induced canine synovitis model.

Grapiprant

- selective EP4-receptor antagonist
- controls pain by blocking EP4-mediated pain caused by inflammatory prostanoid PGE_2
- strong safety profile and predominantly mild, transient gastrointestinal side effects

Bedinvetmab

- anti-NGF monoclonal antibody
- controls pain by blocking excess nerve growth factor (NGF) to reduce pain signaling
- uncommon to very rare label adverse events mostly relate to immune or neurological systems

Methods

In this blinded, randomised, negative controlled, 2-phase parallel design study, 25 dogs underwent intra-articular (IA) injection of kaolin/carrageenan suspension to induce transient synovitis in the stifle joint on study days (SDs) 0 (right stifle) and 28 (left stifle).
Dogs received either grapiprant tablets (2 mg/kg, n=10) or the negative control product (empty hypromellose capsule, n=5) orally once daily in phase 1 on SDs -7 to 1 and in phase 2 on SDs 21 to 29 or bedinvetmab (0.5-1 mg/kg, subcutaneous injection (SC), n=10), on SD -7 in phase 1 and again on SD 21 in phase 2 (Table 1).
Subjective assessments of pain (standing/walking lameness) and inflammation (joint swelling) were performed prior to each IA injection and at 6, 10, 14, 18, 22, 26, 30, 34 and 48 hours post-IA injection (Table 2, Figures 1, 2 and 3). The subjective assessments were summed to generate a total lameness score (0-9, Figure 4). Preliminary results were evaluated descriptively.

Table 1: treatment groups

Treatment group	Phase 1		Phase 2		N
	Treatment	Frequency	Treatment	Frequency	
1	Grapiprant 2mg/kg, oral	Once daily from day -7 to 1	Grapiprant 2mg/kg, oral	Once daily from day 21-29	10
2	Negative control, oral	Once daily from day -7 to 1	Negative control, oral	Once daily from day 21-29	5
3	Bedinvetmab 0.5-1mg/kg, SC	Once on day -7	Bedinvetmab 0.5-1mg/kg, SC	Once on day 21	10

Table 2: subjective assessments (sum designated total score)

Score	Subjective assessments		
	Standing	Weight-bearing at Walking	Joint Swelling
0	Normal	Normal	None
1	Mild shift towards normal leg	Mild lameness	Mild
2	Toe touching	Moderate lameness	Moderate
3	Non-weight bearing	Severe (non-weight bearing or toe touching)	Severe

Results

Grapiprant and bedinvetmab were similarly efficacious in reducing pain and improving weight-bearing compared to the negative control; grapiprant reduced joint swelling better compared to both other treatment groups.

Figure 1: Stacked Bar Graph of Standing Scores by Treatment Group over Time (across Phases)

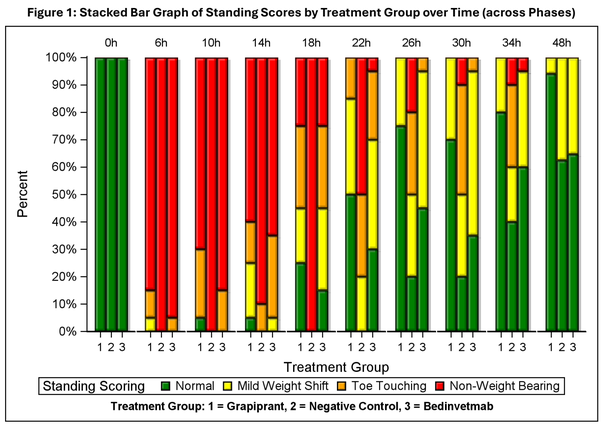


Figure 2: Stacked Bar Graph of Walking Scores by Treatment Group over Time (across Phases)

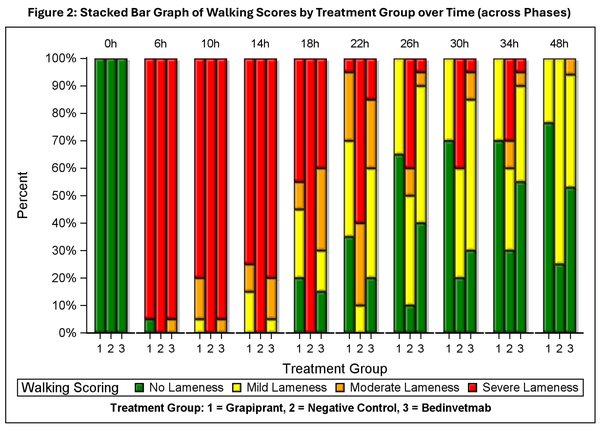
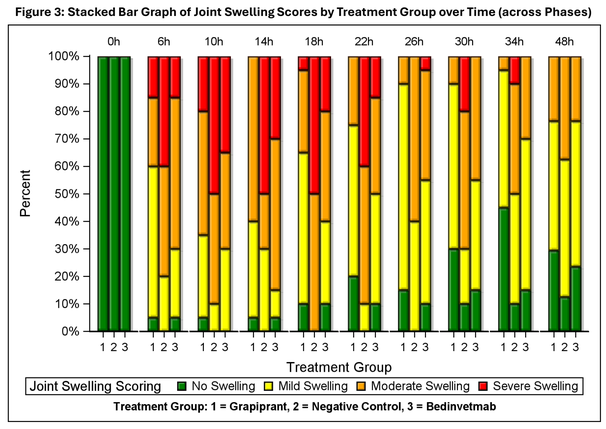
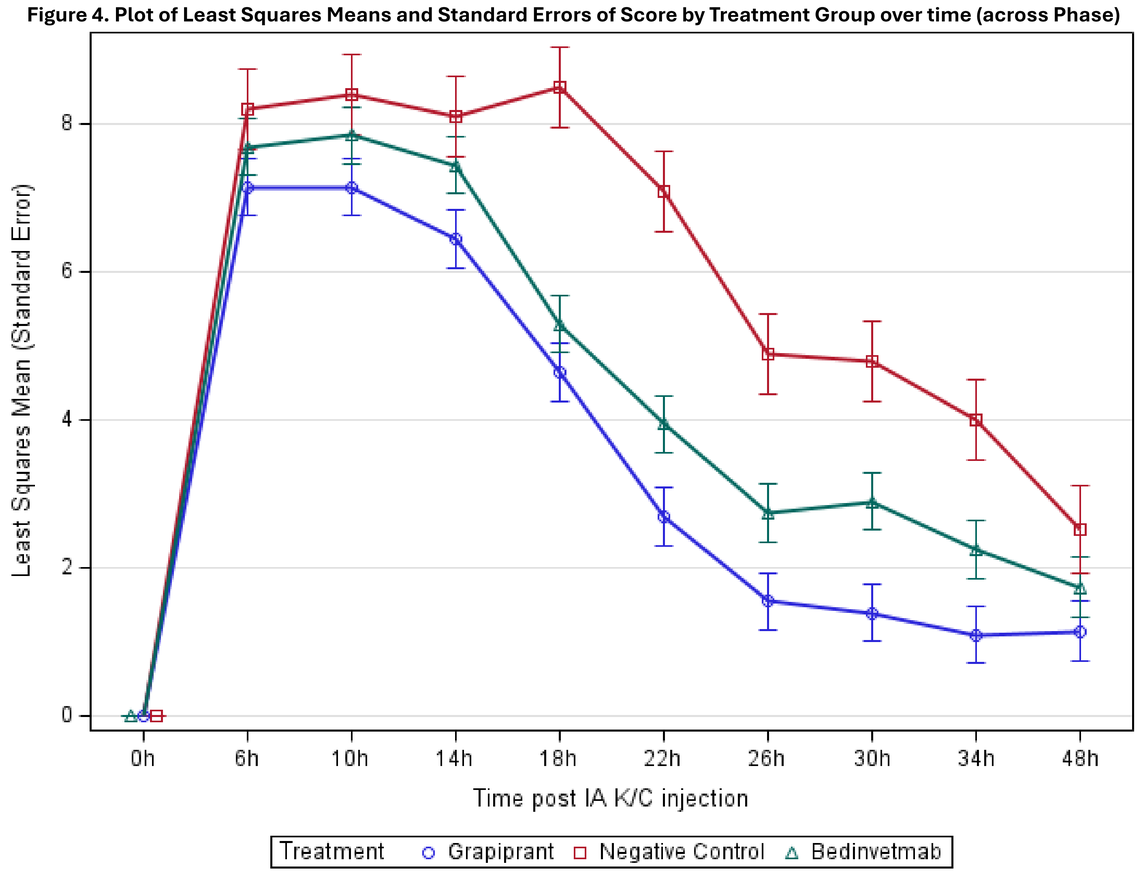


Figure 3: Stacked Bar Graph of Joint Swelling Scores by Treatment Group over Time (across Phases)



Total Scores

Figure 4. Plot of Least Squares Means and Standard Errors of Score by Treatment Group over time (across Phase)



Conclusion

Grapiprant and bedinvetmab were similarly efficacious in reducing lameness, and grapiprant showed a better reduction of inflammation compared to the negative control and bedinvetmab. Additional model study data, including gait analysis, are under further evaluation.
Since control of both inflammation and pain is important in management of osteoarthritis, further investigation of dogs with naturally occurring disease is warranted.