Amorphous calcium carbonate (ACC) as a novel potential treatment for osteoarthritis in dogs: a pilot clinical study

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Background

Osteoarthritis (OA) is a common, degenerative, chronic, and painful joint disease in dogs, characterized by joint acidity, progressive cartilage loss, and abnormal bone remodeling.

Amorphous Calcium Carbonate (ACC; Amorphical Ltd, Israel) is a potential new treatment for canine OA with novel mechanisms based on local pH modulation and targeting bone remodeling, inflammation, and pain.

Due to its unique amorphous (non-crystalline) structure, nanometric size, and pH- dependent solubility, ACC enables local buffering of joint acidity, attenuation of consequent inflammatory joint destruction and impaired bone and cartilage remodeling, while providing highly bioavailable calcium to support adequate bone mineralization.

Together, these properties support the investigation of ACC as a potential disease-modifying therapy, aimed not only at symptomatic relief but also at slowing or altering the structural progression of osteoarthritis.

Objective

To assess the potential efficacy and safety of ACC in dogs with osteoarthritis

Methods

Study Design

- Prospective, randomized, double-blind, placebo-controlled pilot study in 41 client-owned dogs ≥2 years with clinically and radiologically confirmed osteoarthritis, allocated in a 2:1 ratio to ACC: Placebo treatment for 56 days. Visits were performed on day 0, day 14, day 28 and day 56 and included owner assessments of pain, mobility and function using validated questionnaires, and veterinary orthopedic examination.
- No pain or anti-inflammatory drugs were allowed during the study.
- Rescued dogs were considered treatment failures.

Outcome measures- Efficacy

Efficacy was determined by improvement in pain level, mobility and performance of daily activities using validated owner questionnaires. Veterinary assessments included orthopedic examination of OA joints.

Owner assessments:

- **Canine Brief Pain Inventory (CBPI) questionnaire:**
  - Pain level (pain severity score; PSS)
  - Effect of pain on performance of daily activities (pain interference score; PIS)
  - Effect of pain on Quality Of Life (QOL)
- **Canine Specific Outcome Measures (CSOM) questionnaire**
  - Individually selected 3 impaired daily activities (e.g., walking, running, climbing stairs)

Veterinary assessments:

- **Veterinary Orthopedic Score (VOS):** assessing joint pain, lameness, joint swelling and mobility

Outcome measures - Safety

Safety in the study population was monitored by:

- Veterinary physical examination
- Clinical pathology (hematology, biochemistry)
- Adverse event recording

Treatment success - definition

Treatment success of ACC group Vs. Placebo:

Improvement in pain scores on day 56 vs day 0 (CBPI):

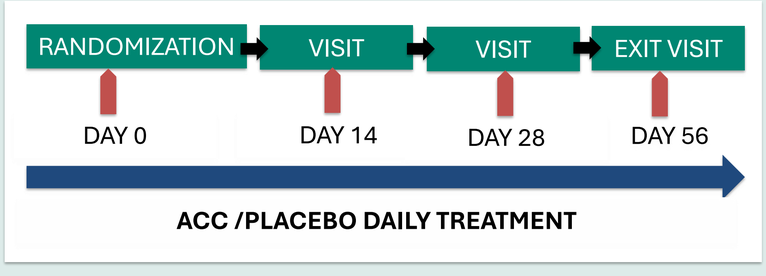
- Decrease in Pain Severity Score (PSS) ≥1, AND
- Decrease in Pain Interference score (PIS) ≤2 and ≤ 1, AND
- QOL same/better

Improvement in mobility scores on day 56 vs day 0 (CSOM):

- Decrease in CSOM score ≥2

Study flow

Figure 1. Study outline



Results

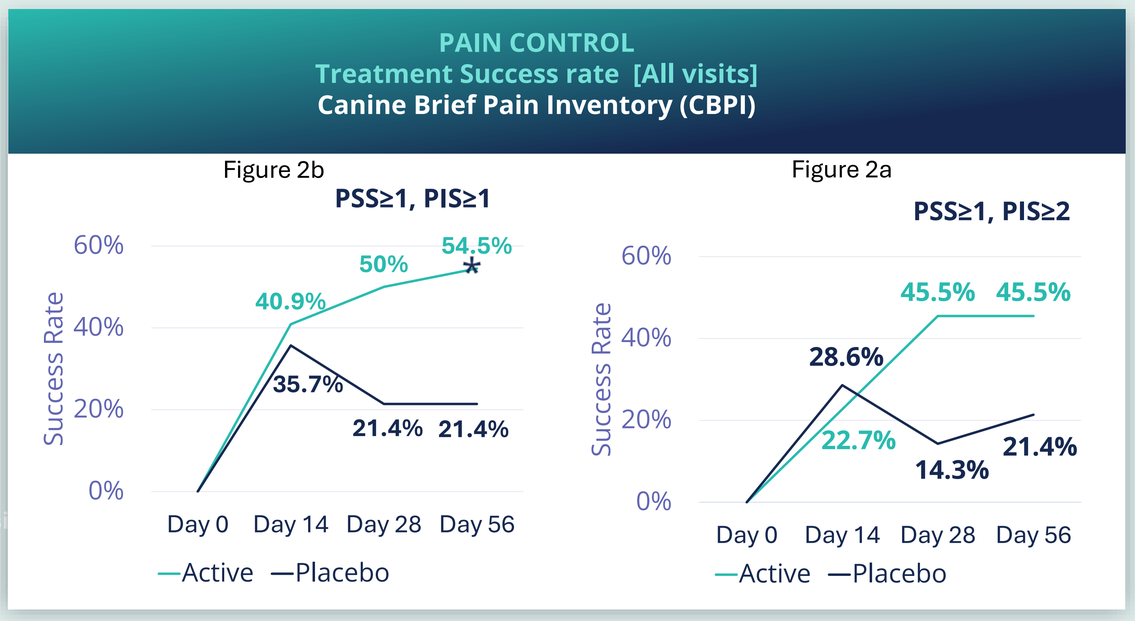
- 53 dogs were screened; 41 enrolled
- 41 (26 ACC:15 Placebo) and 36 (22 ACC: 14 Placebo) were found evaluable for safety (ITT) and efficacy (PP) assessment, respectively
- 21.4% (3/14) of Placebo dogs and 4.5% (1/22) of ACC dogs were rescued due to pain and were considered treatment failures
- On day 56, within the ACC group only, the CBPI, CSOM, and VOS assessments were lower compared to day 0 and day 14 ($p < 0.05$; Table 1)
- On day 56, proportionally more ACC than placebo dogs were treatment successes based on CBPI (PSS ≤1, PIS ≤ 2; $p = 0.1$, Figure 2a) (PSS, PIS ≤ 1; $p=0.05$, Figure 2b) and CSOM ($p = 0.06$, Figure 3)

Safety

- No serious adverse events or clinically significant treatment-related effects were recorded in the study
- There were no treatment-related changes in clinical pathology results, including serum calcium and phosphorus levels
- Two mild, transient cases of soft stool/diarrhea were recorded in the study. Their proportion was similar between ACC and placebo dogs (7.7% and 6.6%, respectively)

Efficacy: PAIN CONTROL

Figure 2. Percentage of dogs classified as Treatment Success for pain control



Efficacy: MOBILITY CONTROL

Figure 3. Percentage of dogs classified as Treatment Success for mobility control

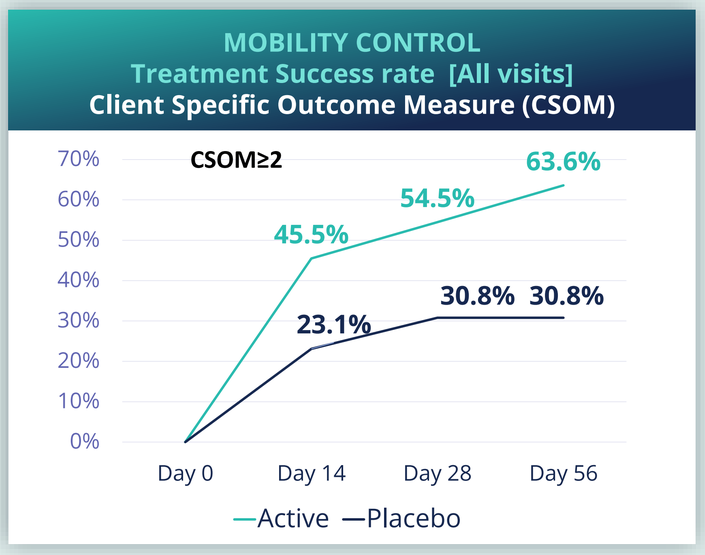


Table 1. Within treatment analysis for PSS, PIS, CSOM and VOS at all visits

	Pain Severity Score, PSS (Mean ± SD)		Pain Interference Score, PIS (Mean ± SD)		Client Specific Outcome Scores, CSOM (Mean ± SD)		Veterinary Orthopedic Scores, VOS (Mean ± SD)	
	Amorphous Calcium Carbonate (ACC)	Placebo	Amorphous Calcium Carbonate (ACC)	Placebo	Amorphous Calcium Carbonate (ACC)	Placebo	Amorphous Calcium Carbonate (ACC)	Placebo
	(N = 22)	(N = 14)	(N = 22)	(N = 14)	(N = 22)	(N = 13)	(N = 22)	(N = 14)
Baseline	4.35 (± 1.13)	4.63 (± 1.85)	5.50 (± 1.47)	5.30 (± 1.77)	10.0 (± 1.88)	10.5 (± 1.33)	6.54 (± 2.74)	7.07 (± 2.65)
Day 14	3.56 (± 1.93)[a]	3.67 (± 1.92)	3.91 (± 2.09)[a]	4.46 (± 1.96)	8.55 (± 2.67)[a]	9.54 (± 1.71)	5.00 (± 2.31)[a]	4.79 (± 3.17)
Day 28	3.33 (± 1.68)[a]	3.79 (± 2.29)	3.54 (± 2.11)[a, b]	4.42 (± 2.49)	8.00 (± 2.53)[a]	9.00 (± 2.16)	3.82 (± 2.94)[b]	4.93 (± 3.17)
Day 56	2.75 (± 1.78)[b]	3.88 (± 2.13)	3.19 (± 2.30)[b]	4.06 (± 2.30)	7.45 (± 2.70)[b]	8.77 (± 2.32)	3.91 (± 2.86)[b]	4.29 (± 3.36)

Mean (± standard deviation)
Repeated measures analysis of variance with Baseline as a covariate)
[a, b] different letters represents significantly different means ($p < 0.05$)

Conclusions

- ACC was found safe in the study population.
- The study results support the conduct of larger studies to confirm whether ACC may be a safe and effective treatment for osteoarthritis in dogs and potentially a disease-modifying drug

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