ABSTRACT NUMBER: 0636

Evidence of a Dose-Response Relationship in a Phase 2b Study of a Fixed-Dose Combination of Apocynin and Paeonol in Knee OA Patients With Moderate to Severe Pain and Nociplastic Pain Features

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SESSION INFORMATION

Date: Sunday, November 8, 2026

Session Type: Poster Session A

Title: (0632-0644) Osteoarthritis - Clinical Poster A

Session Time: 10:30AM-12:30PM

Background/Purpose: Current treatments for OA are limited to symptoms and associated with poor efficacy or serious safety risks, therefore, there is a great unmet need for new OA therapies.

As a promising investigational product, a fixed-dose combination of apocynin and paeonol in a ratio of 2:7 (APPA) was previously evaluated in a Phase 2a trial, where it was associated with positive signals of efficacy in symptomatic OA patients with possible nociplastic pain features, but the trial was limited by short duration of treatment, and a single APPA dose regimen.

This report describes the results of the subsequent phase 2b trial addressing the potential limitations of the Ph2a trial.

Methods: The trial was a randomized, double-blind, placebo-controlled trial where a total of 225 participants were randomized 1:1:1 between oral APPA 800 or 1200 mg, or placebo twice daily for 12 weeks.

The main inclusion criteria were radiographic knee OA with a KL-grade 2 or 3, WOMAC pain score ≥50 and ≤90/100, and a PainDETECT score of ≥13 out of 38. The main exclusion criteria included recent intraarticular interventions, and BMI ≥40 kg/m2. The primary endpoint was the change from baseline to Day 84 in the WOMAC pain score. Key secondary endpoints included Weekly Average of Daily Pain

(WADP), ICOAP, other WOMAC domains, PGA, OMERACT-OARSI Responders, and EQ-5D. Safety outcomes included adverse events (AE), lab parameters, ECG, and vital signs.

Detailed pharmacokinetics (PK) were assessed in a substudy involving 24 patients.

Pre-planned subgroup analyses included participants with higher baseline pain scores.

The efficacy analyses were performed in the mITT population and relevant subgroups by an MMRM (continuous variables), including relevant covariates, and binary outcomes by a logistical regression

Results: A total of 225 participants were randomized, of which 205 (91.1 %) completed the trial. The main baseline demographics are shown in Table 1.

The main efficacy outcomes are illustrated in Figure 1.

For the primary endpoint, there was no statistically significant difference in WOMAC pain between APPA and placebo. Among the secondary endpoints, a consistent signal indicating a dose-dependent beneficial effect of APPA was observed in WADP and ICOAP.

In the pre-planned subgroup analysis of participants with higher WOMAC pain at baseline, a consistent, dose-dependent, and in the highest APPA dose group, for several outcomes, statistically significant benefit was observed across most endpoints.

The safety and tolerability of APPA was generally good, with the most frequently reported AE being transient mild GI discomfort.

Preliminary assessments of PK indicated large variability in the absorption of APPA (data not shown).

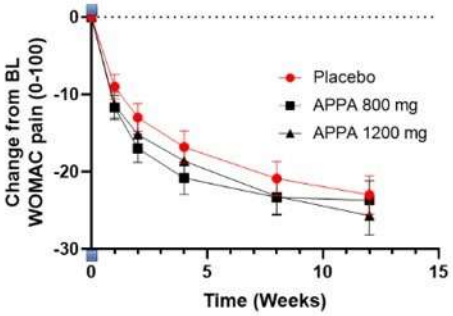
Conclusion: In this phase 2b trial, APPA was not associated with a significant improvement in WOMAC pain compared to placebo, however signals of efficacy were observed in other efficacy endpoints. Subgroup analysis of participants with higher baseline pain provides evidence of a clinically relevant efficacy of APPA 1200 mg in this population, warranting further research. APPA was well tolerated and safe.

Table 1: Baseline Demographics

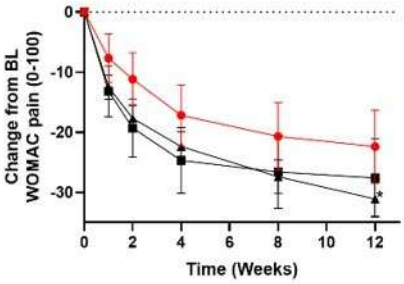
	Placebo twice daily	800 mg APPA twice daily	1200 mg APPA twice daily
	(N=77)	(N=72)	(N=75)
Age			
Mean (SD)	63.3 (8.2)	64.0 (7.9)	64.6 (7.9)
Sex			
Male	38 (49.4%)	26 (36.1%)	31 (41.3%)
Extent of knee OA			
Bilateral	69 (89.6%)	67 (93.1%)	66 (88.0%)
BMI			
Mean (SD)	27.9 (4.4)	28.4 (4.7)	28.3 (4.1)
PainDETECT baseline score			
Mean (SD)	17.2 (3.6)	17.8 (3.8)	17.7 (3.0)
WOMAC pain baseline - target knee			
Mean (SD)	32.2 (4.7)	31.8 (5.0)	32.3 (4.4)

Table 1: Baseline Demographics

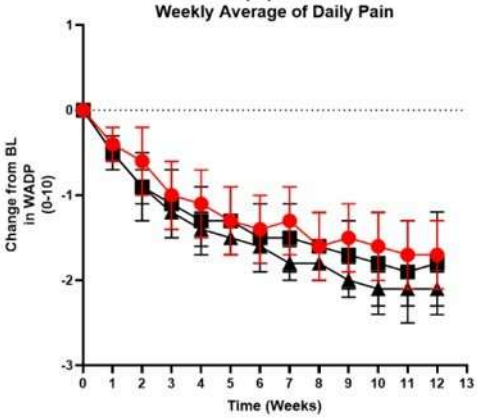
ITT population
WOMAC pain



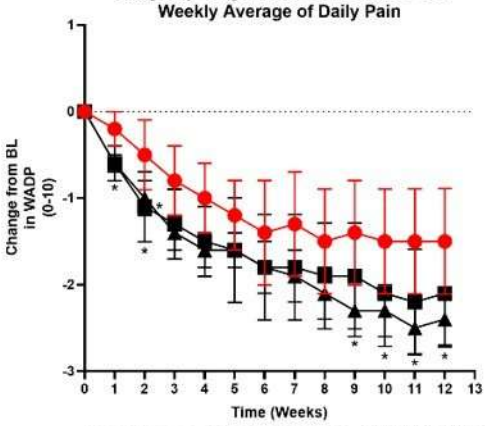
Subgroup Target Knee BL WOMAC > 30
WOMAC Pain



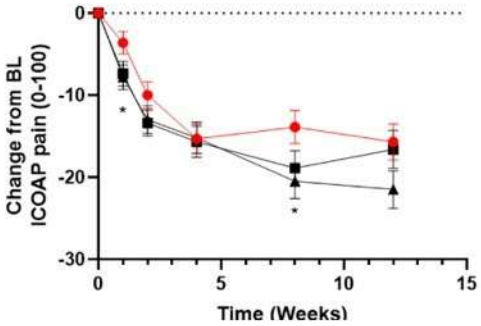
ITT population
Weekly Average of Daily Pain



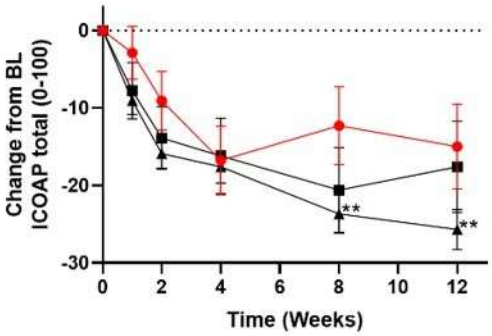
Subgroup Target Knee BL WOMAC > 30
Weekly Average of Daily Pain



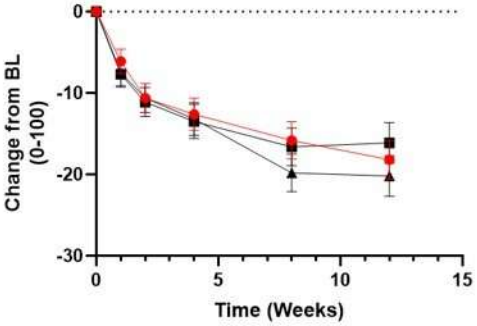
ITT population
ICOAP Total



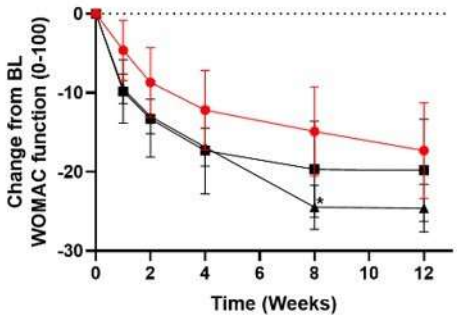
Subgroup Target Knee BL WOMAC > 30
ICOAP Total



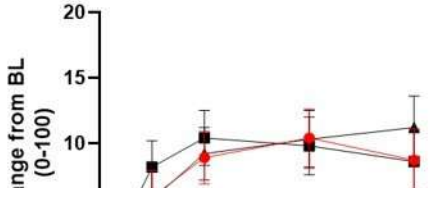
ITT population
WOMAC Function



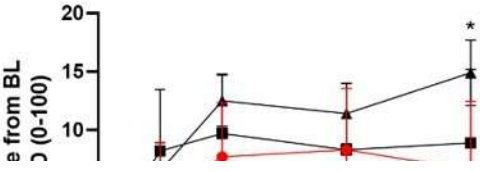
Subgroup Target Knee BL WOMAC > 30
WOMAC Function



ITT population
EQ-5D VAS



Subgroup Target Knee BL WOMAC > 30
EQ-5D



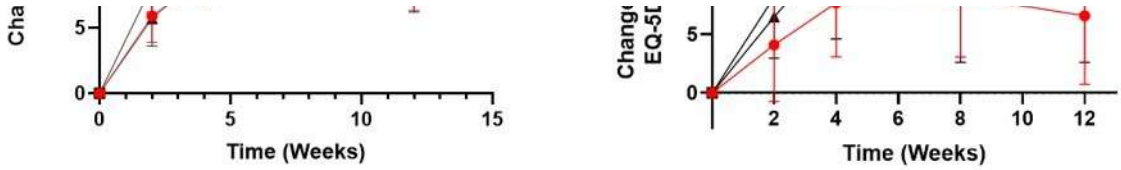


Figure 1: Overview of main efficacy outcomes in the ITT population, and in the subgroup of participants with baseline WOMAC pain > 30 out of 50

Disclosures: A. Bihlet: NBCD A/S, 12,; **N. Petersen**: NBCD A/S, 12,; **A. Kaaber**: None; **E. Petersen**: NBCD A/S, 12,; **H. Rovsing**: None; **P. Alexandersen**: None; **S. Larsen**: None; **E. Lau**: None; **D. Miles**: AKL Research and Development Ltd, 12,; **A. Reynolds**: AKL R&D Ltd, 12,, 12, , 10; **P. Conaghan**: AbbVie/Abbott, 12,, AstraZeneca, 12,, Biosplice, 12,, Eli Lilly, 12,, Formation Bio, 12,, Genascence, 12,, Genascence Corporation, 12,, Grunenthal, 12,, Kolon TissueGene, 12,, Levicept, 12,, Moebius, 12,, Novartis, 12,, Pacira, 12,, Stryker, 12,.

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