Characterizing Pain Rescue Medication Use in Knee Osteoarthritis Trials – a Post-hoc Analysis

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Background

- Many osteoarthritis (OA) trials allow controlled use of rescue medication (RM), commonly paracetamol, with various restrictions.
- The purpose of RM is to offer pain relief for participants on placebo or if the investigational product is ineffective.
- Poor control of RM use may affect the interpretation of trial results and contribute to explaining PR.

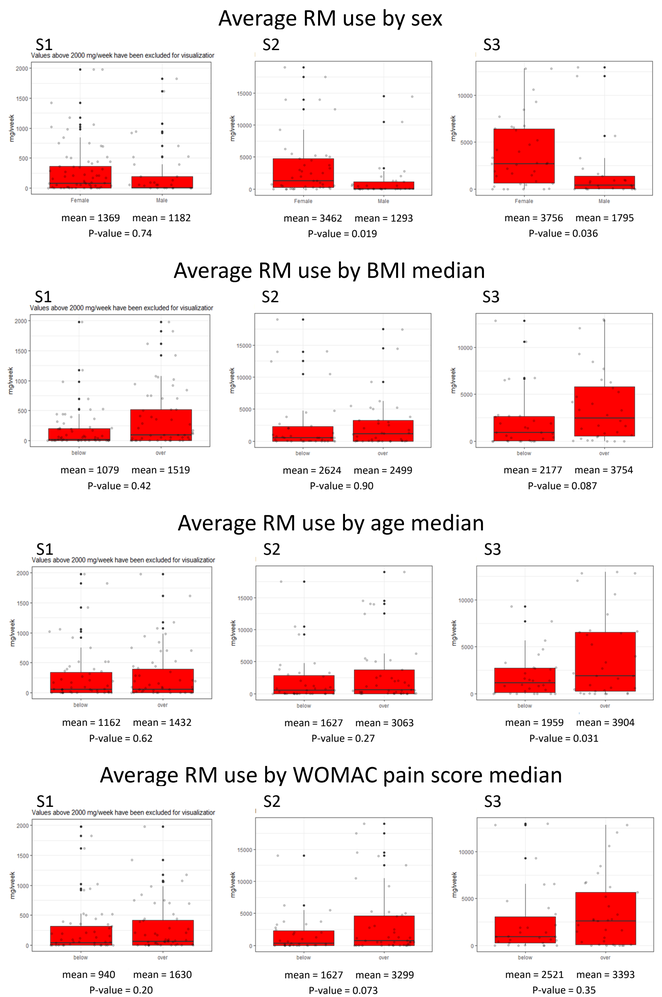
Aim

- To identify typical RM usage patterns and explore associations with clinical and demographic characteristics in OA trials.

Methods

- This is a post-hoc analysis of three phase 2, multicenter, randomized, double-blind, placebo-controlled trials for knee OA in adults[1-3].
- These 3 studies involved a total sample size of 638.
- The population was a typical knee OA population in terms of radiographic severity and WOMAC pain score.
- We analyzed the participants receiving placebo.
- Tests for differences on dichotomization were done with two-sided t-tests.
- Multivariate relationships with use of RM among variables were analyzed using multiple regression; RM doses were logarithmically transformed for normal distribution.

In knee osteoarthritis trials, **female sex and greater BMI** are associated with **higher use** of rescue medication.



Results

- 283 participants receiving placebo completed
- Baseline demographics include overall mean (SD):
  - Age 61.1 (8.5) years
  - Female sex 60.8%
  - BMI 30.7 (5.0) kg/m^2
  - WOMAC pain score 34.2 (8.5)
- RM usage:
  - 68.6% took at least 1 dose during the study
  - Average use for RM users was 2656 mg/week
  - Average use for population was 1876 mg/week

Relevance for Clinical Trials

- RM use characterization is important for accurately interpreting trial results.
- Helps differentiate between the effects of the investigational medicinal product and additional pain relief measures.
- Crucial for designing trials that identify true treatment effects.
- Contributes to improve trial design and advance patient care by addressing RM use.

References

1. Bihlet AR, et al. Efficacy and safety of an intra-articular placental tissue particulate (MOTYS/PTP-001) in symptomatic knee osteoarthritis over 26 weeks: A placebo-controlled, double-blind randomized clinical trial. Osteoarthritis Cartilage. 2024 Apr.
2. Bihlet AR, et al. POS0104 A PHASE 2B DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMIZED CLINICAL TRIAL OF SB-061, AN AGGRECAN MIMETIC, IN SUBJECTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS. In: Scientific Abstracts. BMJ Publishing Group Ltd and European League Against Rheumatism; 2023.
3. Bihlet AR, et al. The efficacy and safety of a fixed-dose combination of apocynin and paeonol, APPA, in symptomatic knee OA: A double-blind, randomized, placebo-controlled, clinical trial. Osteoarthritis Cartilage. 2024 Apr.
- Zhang W, et. al. The placebo effect and its determinants in osteoarthritis: meta-analysis of randomised controlled trials. Ann Rheum Dis. 2008 Dec.
- Bannuru RR, et. al. Effectiveness and Implications of Alternative Placebo Treatments. Ann Intern Med. 2015 Sep.
- Karsdal MA, et. al. Disease-modifying treatments for osteoarthritis (DMOADs) of the knee and hip: lessons learned from failures and opportunities for the future. Osteoarthritis Cartilage. 2016 Dec.
- Huang Z, et al. Meta-analysis of pain and function placebo responses in pharmacological osteoarthritis trials. Arthritis Res Ther. 2019 Dec.
- Zeidler H. Paracetamol and the Placebo Effect in Osteoarthritis Trials: A Missing Link? Pain Res Treat. 2011 Jun.