Advil

HALEON

Ibuprofen outperforms Acetaminophen in Osteoarthritis pain relief: Clinical evidence supports single-dose and 14-day multiple-dose efficacy

Results from a multicenter, randomized, double-blind, parallel-group comparative study conducted in patients with knee or hip OA

Boureau, F., Schneid, H., Zeghari, N., Wall, R., & Bourgeois, P. (2004).
The IPSO study: ibuprofen, paracetamol study in osteoarthritis. A randomised comparative clinical study comparing the efficacy and safety of ibuprofen and paracetamol analgesic treatment of osteoarthritis of the knee or hip
Annals of the rheumatic diseases, 63(9), 1028-1034.

Background

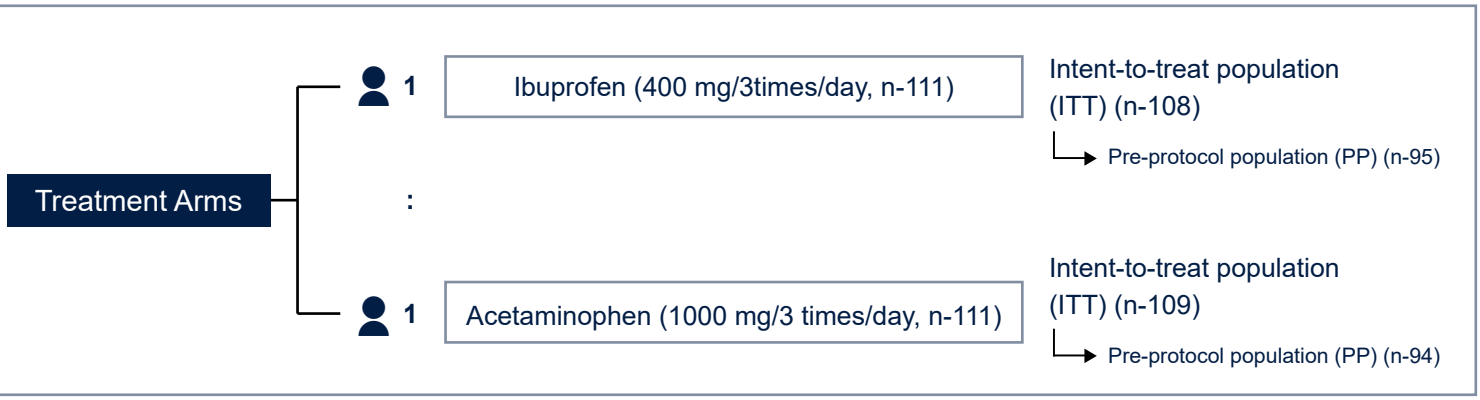
- Osteoarthritis (OA) is the most common form of joint disease and is an important public health concern. Oral nonsteroidal anti-inflammatory drugs (NSAIDs) are highly effective and widely recommended for OA pain of the knee, hand, and/or hip
- A study by Bradley et al suggested that ibuprofen (IBU), administered at high doses (2400 mg/day) or low doses (1200 mg/day), is equally effective as acetaminophen (APAP) (4000 mg/day) in alleviating knee OA pain[1]. In addition, a double-blind 6-day study found ibuprofen (1200 mg/day) at least as effective as paracetamol (4000 mg/day) in the treatment of knee OA pain, and better than paracetamol in subjects with moderately severe or severe baseline pain[2]
- The American College of Rheumatology (ACR) 2019 Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee 'strongly' recommends oral NSAIDs like ibuprofen, and 'conditionally' recommends acetaminophen[3]

Study Objective

To compare the analgesic efficacy of single and multiple doses of IBU with that of APAP in patients with knee or hip OA over 14 days using the pain intensity assessment, functional disability assessment, and patient global assessment

Study Design and Methodology

Two-week, multicenter, randomized, double-blind, parallel-group comparative study conducted in patients ages 50-85 years with knee or hip OA



Eligibility Criteria

- Patients of either sex with chronic pain (score at least 50 mm on a 100 mm visual analogue scale (VAS)) due to confirmed knee or hip OA and requiring analgesic treatment
- A washout period of up to 3 days if NSAIDs and/or analgesics had been taken within 72 hours and 8 hours, respectively, of the pre-inclusion visit
- Patients with painful OA of the lower limbs (femorotibial or femoropatellar knee/hip OA) diagnosed according to the criteria from the American College of Rheumatology (ACR) clinical and radiological criteria.

Key efficacy outcomes

Sum of pain intensity difference scores (SPID) on a 100 mm VAS every hour over 6 hours after the first administration of treatment

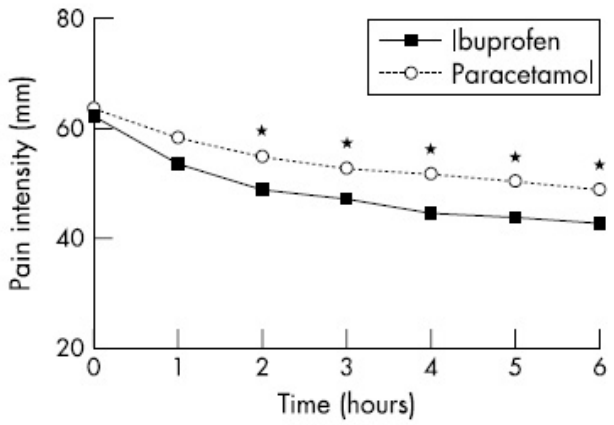
Secondary outcomes

- Assessment related the pain intensity (PI), the PID, and the peak PID over 0-6 hours
- Daily pain average intensity(PI) 0-13th day of treatment
- The global efficacy of the treatment
- Functional disability assessed using the WOMAC

Results

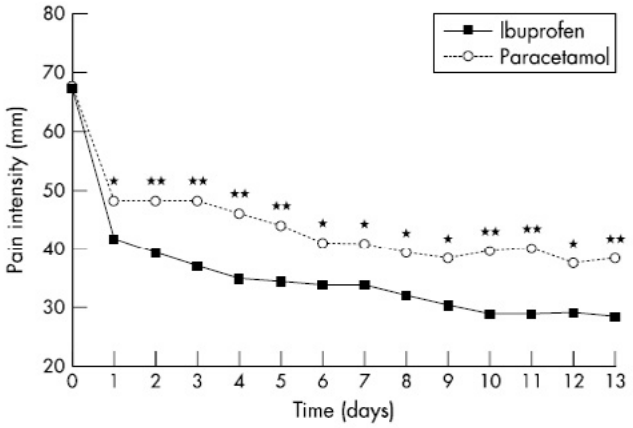
Patients treated with IBU reported greater pain relief as compared to APAP within hours on the first day which persisted over a 14-day period

Pain intensity during 0-6 hr after first dose



Evolution of the pain intensity during 6 hours after the first dose. *p < 0.05, Student's t test.

Pain intensity over 14 days of treatment

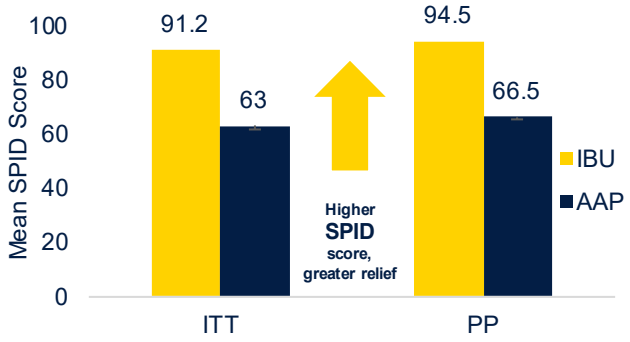


Evolution of the pain intensity over 14 days of treatment assessed by a VAS. *p<0.05; **p < 0.005, Student's t test.

The pain intensity difference significantly favored IBU over APAP over the first 6 hours (p=0.046) and over the period of 14 days (p<0.05) independent of the type of joint

IBU provides a more marked significant reduction in pain as compared to APAP over 6 hours after the first administration

SPID over 6 hours from baseline

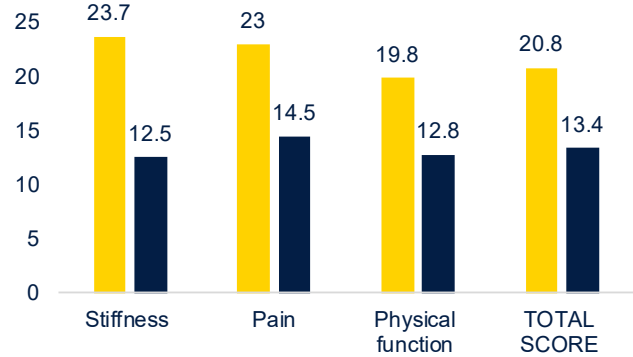


IBU group has a higher SPID score compared to APAP group

- ITT population (-91.2 Vs -63.0; p = 0.046)
- PP population (-94.5 Vs -66.5, p = 0.069)

Patients receiving IBU demonstrated significant improvement in overall WOMAC score over a two-week treatment period

Reduction in functional disability scores based upon WOMAC

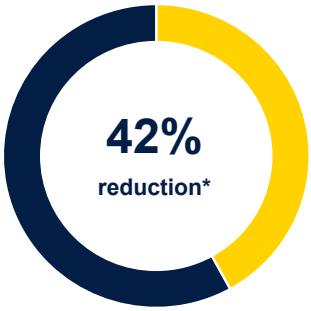


IBU group had significant*:

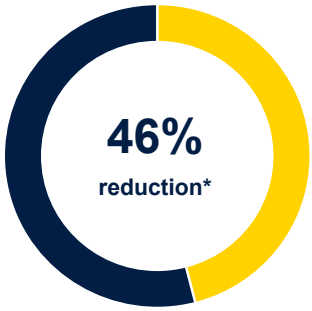
- Less pain (p <0.001)
- Improved stiffness(p=0.002), physical function (p=0.002) and overall functional disability

* compared with the APAP group after 2 weeks of treatment

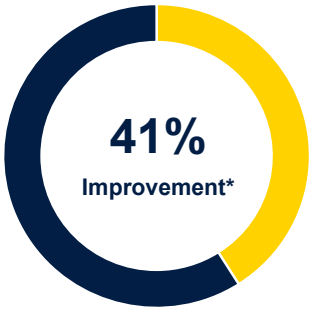
WOMAC Stiffness



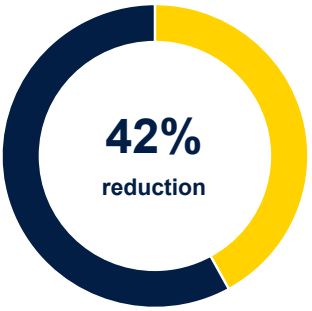
WOMAC Pain



WOMAC Physical function

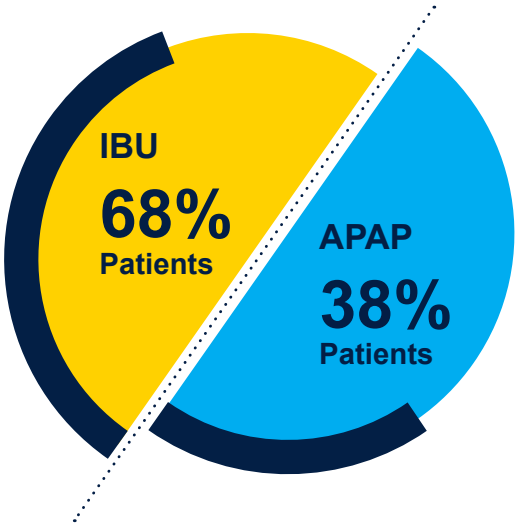


OVERALL Functional Disability



* compared to baseline

“Good to very good” patients rating of global efficacy



IBU was found to be a more favorable choice with better global efficacy

Safety

The incidence of adverse events (AEs) was predominantly mild or moderate in both treatment groups, with no statistically significant difference between the groups. Notably, no serious AEs were reported

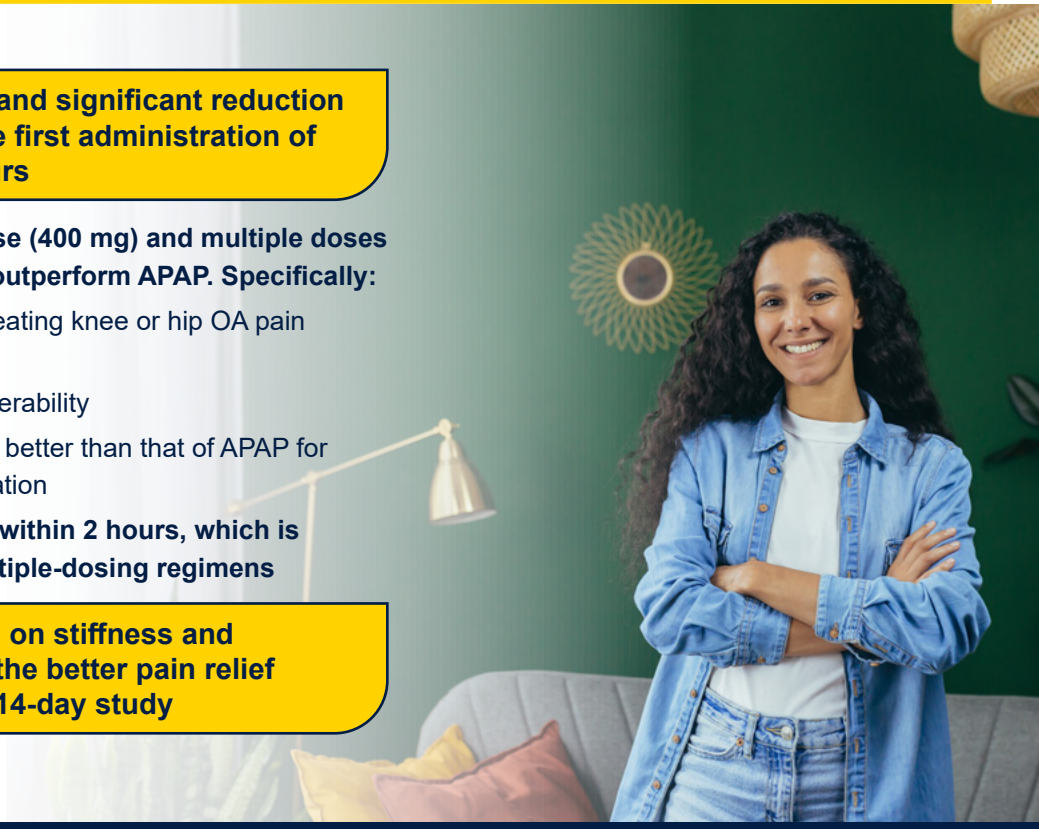
- 51 participants (23%) experienced AEs considered to be potentially related to the treatment with 26 (23.4%) in the IBU group and 25 (22.5%) in the APAP group
- The most common adverse events (AEs) were related to the body as a whole system (20 patients) and the digestive system (24 patients), the most common AEs included nausea, abdominal pain, dyspepsia, and dizziness; among these, only three AEs were severe (2 cases of asthenia and 1 case of pain)

Conclusion

IBU exhibited a more pronounced and significant reduction in pain compared to APAP after the first administration of the study drug, over the first 6 hours

- **IBU administered at both a single dose (400 mg) and multiple doses (1200 mg/day) over a 14-day period, outperform APAP. Specifically:**
  - » IBU is more effective than APAP in treating knee or hip OA pain starting from day 1
  - » Both IBU and APAP exhibit similar tolerability
  - » The efficacy/tolerability ratio of IBU is better than that of APAP for treating OA pain over the 14-day duration
- **IBU offers a rapid onset of analgesia within 2 hours, which is sustained throughout the 14-day multiple-dosing regimens**

The greater beneficial effect of IBU on stiffness and functional disability was linked to the better pain relief achieved with IBU throughout the 14-day study



References

1. Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. (1991). N Engl J Med;325:87–91.
2. Altman RD. (1999). Arthritis Rheum;42(suppl):S403.
3. Kolasinski, S. L., Neogi, T., Hochberg, M. C., Oatis, C., Guyatt, G., Block, J., ... & Reston, J. (2020). 2019. Arthritis & rheumatology; 72(2): 220-233.

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