EP-104IAR (EXTENDED-RELEASE INTRA-ARTICULAR INJECTION OF FLUTICASONE PROPIONATE) SHOWS SUSTAINED PAIN RESPONSE FOR SUBJECTS WITH MODERATE BASELINE PAIN AND BMI LESS THAN 30 IN SPRINGBOARD, A PHASE 2, RANDOMIZED, 24-WEEK STUDY OF OSTEOARTHRITIS OF THE KNEE

Poster #635

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Background

- Knee osteoarthritis (KOA) is a major and growing cause of pain and disability.
- Patients with moderate KOA pain, not suitable for surgery, have unmet medical need as they are prescribed more pain medication yet report lower treatment satisfaction and decreased quality of life compared to patients with mild pain.[1] High BMI is a risk factor for KOA pain, potentially treatable with GLP-1 agonists, however, patients with BMI <30 not eligible for GLP-1 agonists present another potential unmet medical need.
- Recommended treatment includes intra-articular (IA) corticosteroids, however, these have limited duration of effect and risk of side effects.
- EP-104IAR is a novel long-acting fluticasone propionate (FP) IA injection that employs a controlled-release technology designed to optimize the pharmacokinetics of FP, maximizing IA residence time while limiting systemic exposure, providing potentially greater duration of efficacy with fewer systemic side effects (Fig 1).

Aim

- We present the results of subgroup efficacy analyses of SPRINGBOARD, a Phase 2, randomized, double-blind, vehicle-controlled, parallel-group study of EP-104IAR (NCT04120402).
- Analysis subgroups were defined post-hoc, composed of patients with moderate baseline WOMAC pain scores (3.5-6.5) and those with baseline BMI <30.

Methods

- The study enrolled patients ≥40 years, with primary KOA K-L Grade 2 or 3, OA symptoms for ≥6 months and weekly WOMAC pain scores ≥4.0 to ≤9.0 (out of 10) which did not vary by >3 points within the screening period.
- Subjects were randomized 1:1 to receive a single IA dose of EP-104IAR 25mg (163) or vehicle (155) in one index knee and were followed for 24 weeks.
- 105 subjects who received EP-104IAR and 109 who received vehicle had moderate baseline WOMAC pain scores (3.5-6.5); 88 subjects who received EP-104IAR and 80 who received vehicle had BMI <30.
- Weekly WOMAC pain scores were collected and a mixed-effects model for repeated measures (MMRM) was fit to the change from baseline. The proportion of pain responders, defined as ≥50% decrease from baseline with absolute decrease ≥2 was calculated.

Results

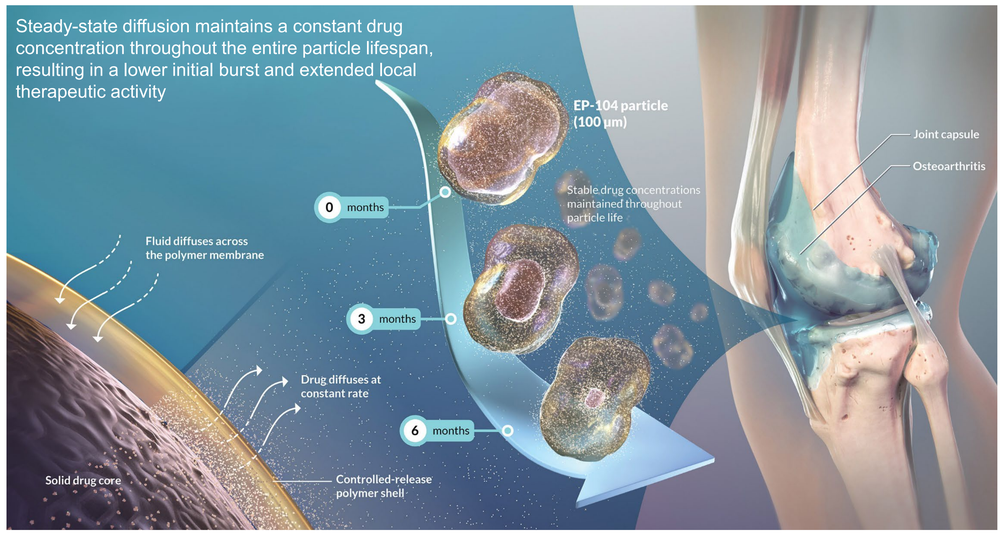

Figure 1: Schematic of EP-104IAR mechanism of action

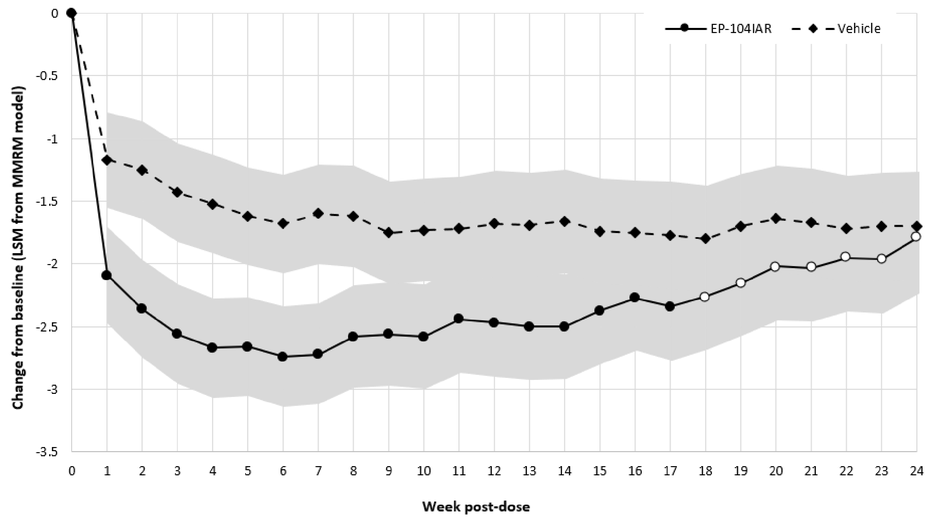

Figure 2: Change from baseline in WOMAC pain for the moderate pain at baseline subgroup
Note: Solid dots indicate p<0.05 in LS mean difference, open dots indicate p≥0.05. Shaded areas indicate 95% CI

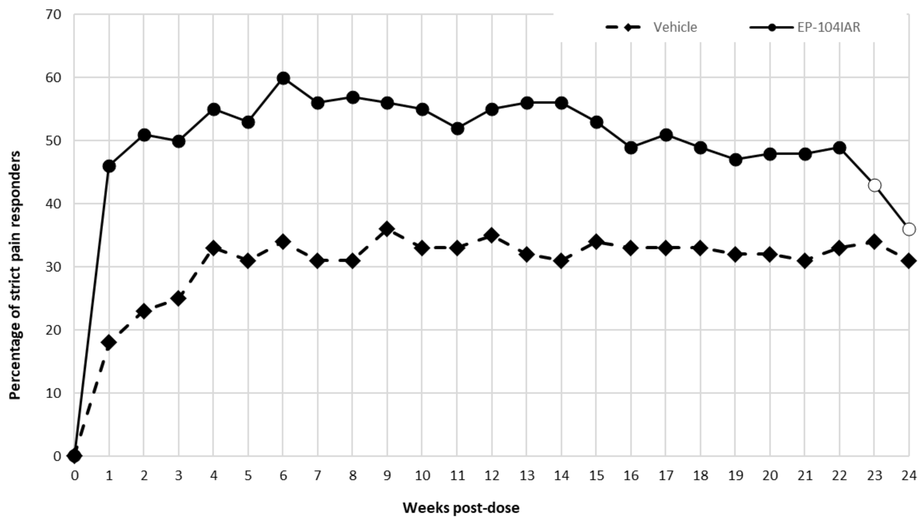

Figure 3: Frequency of pain responders in the moderate pain at baseline subgroup
Note: Pain response was defined as a decrease from baseline in WOMAC pain of at least 50% and 2 points. Solid dots: p<0.05

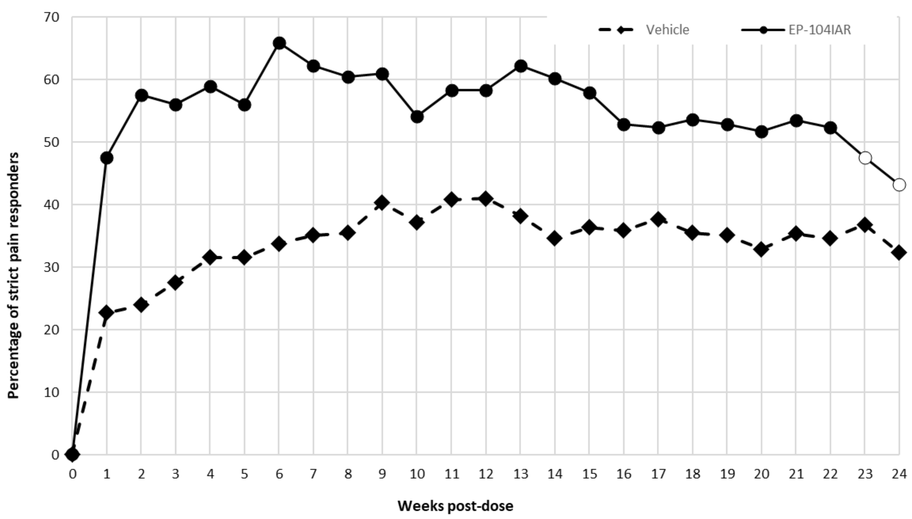

Figure 4: Frequency of pain responders in the BMI <30 at baseline subgroup
Note: Pain response was defined as a decrease from baseline in WOMAC pain of at least 50% and 2 points. Solid dots: p<0.05

Results

- EP-104IAR was well tolerated, without drug-related SAEs or discontinuations.
- FP concentrations were maintained at 66-33% of peak to Week 24.
- A minority of participants had shifts to low serum cortisol which normalized by Week 2 in most cases.
- Changes in glucose for participants with NIDDM were minimal and similar to the overall population; no participants developed adrenal insufficiency.
- Clinically meaningful symptom benefit vs vehicle control was observed in pre-specified primary and key secondary endpoints of change from baseline in WOMAC pain at Week 12, change from baseline in WOMAC function at Week 12, and area-under-the-curve for WOMAC pain to Week 24.[2]
- In the moderate pain subgroup, change from baseline in WOMAC pain at each week showed a statistically significant difference between EP-104IAR and vehicle to Week 17 (Fig 2). In the BMI <30 subgroup, change in pain was significantly greater at 17/24 timepoints including at Weeks 21 and 22 (not shown).
- The frequency of pain responders was significantly greater in the EP-104IAR arm to Week 22 in both the moderate pain and BMI <30 subgroups (Fig 3 and 4).
- These results showed greater separation between the EP-104IAR and vehicle control arms than in the overall population.[3]

Conclusions

- In this subgroup analysis of patients with moderate baseline pain and/or BMI <30, a single dose of EP-104IAR provided statistically significant improvement in WOMAC pain at timepoints beyond 12 weeks post-dose.
- This analysis reinforces the potential for EP-104IAR to deliver sustained clinically meaningful benefit in KOA.
- Findings are particularly relevant for patients with moderate pain and/or reduced risk of progression to severe pain who may require treatment for a longer period of time before progressing to surgical intervention.
- Phase 3 trials of EP-104IAR are now planned.

References

1. J Pain Res 2021; 14:2313-26
2. Lancet Rheumatol 2024; https://doi.org/10.1016/S2665-9913(24)00223-6A
3. ACR Convergence 2023; Abstract L04

Disclosures & Contact Information

AM, JH, MMK, CD, VP, and AD are employees of Eupraxia Pharmaceuticals. SLB, HR, and KM are or were employees of Sanos Clinics who were contracted by Eupraxia Pharmaceuticals to perform the clinical research. ACM, YL, CPM, and ARB are employees of NBCD, a contract research organisation contracted by Eupraxia Pharmaceuticals to perform data management and trial management. MW is on the Board of Directors for Eupraxia Pharmaceuticals and received royalties from NextStep Arthropedix. LSS has no relationships, activities, or interests to disclose. PGC has performed speakers' bureaus or consultancies for AbbVie, AstraZeneca, Eli Lilly, Eupraxia, Galapagos, Genascence, GSK, Grunenthal, Janssen, Levicept, Medipost, Merck, Moebius, Novartis, Sandoz, Stryker, TrialSpark, and UCB.

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