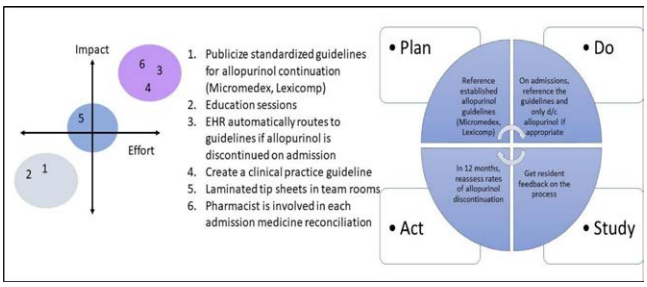

Figure 1. Countermeasures and Implementation Plan

Conclusion: There is evidence of inappropriate discontinuation of allopurinol that leads to gout flares in the outpatient setting and unnecessary resource utilization. We developed an implementation plan to mitigate this systematically at an institutional level. Testing these recommendations next to devise a standardized protocol as a continuous improvement strategy may help improve gout care and patient outcomes.

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OP0170

PHASE 2A, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF THE EFFICACY AND SAFETY OF A TRANSDERMAL ALKALINIZING AND PAIN-RELIEVING TREATMENT FOR REDUCING PAIN ASSOCIATED WITH AN ACUTE GOUT FLARE

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Background: Monosodium urate (MSU) deposition is pathognomonic for gouty arthropathy. MSU crystal formation and dissolution is affected by pH and theoretically, alkalinizing agents (eg, sodium bicarbonate, $NaHCO_3$) that raise the joint microenvironment pH, could facilitate MSU crystal dissolution[1] and decrease the pain of an acute gout flare. However, oral $NaHCO_3$ use is fraught with intolerable gastrointestinal side effects.

Objectives: To determine if $NaHCO_3$ in a patented transdermal formulation could effectively and safely reduce the pain of an acute gout flare.

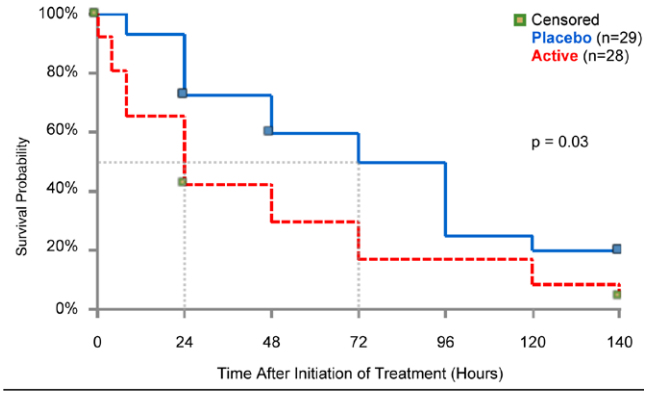
Methods: A Phase 2a prospective, double-blind, randomized, placebo-controlled study enrolled 418 subjects across 20 US sites. Patients with a diagnosis of gout using ACR/EULAR criteria (Score ≥ 8), ages 18-75, history of ≥ 2 gout flares in 12 months prior to randomization and on stable doses of urate lowering therapy were included. Exclusion criteria were BMI > 40kg/m^2, > 12 gout flares in the year prior to randomization, history of rheumatoid arthritis, psoriatic arthritis, evidence of septic arthritis, acute polyarticular gout (≥ 4 joints), and arthritis of any other cause. Patients were randomized to receive placebo lotion or transdermal $NaHCO_3$. Upon flare they initiated colchicine (1.2 mg followed by 0.6 mg 1 hour later) and applied study product to the limb of the affected joint. Outcome measures included pain-numeric rating scale (NRS, 0-10), time to resolution of pain (50% reduction), rescue medication use, joint tenderness, and physical function (PROMIS PF-20). Data were collected in patient diaries for the pain and PROMIS measures at several time points from baseline through Day 7, as were adverse events. Statistical analyses utilized ANCOVA (baseline pain as a covariate), Kaplan-Meier curves for homogeneity, and two-proportion z-test, all with α=0.05.

Results: 98 patients had a gout flare during the 14-month study period. Those in the active arm (ITT, N=48) had an overall responder rate of 94.5% vs. 79.3% (p=0.01) in the placebo arm (ITT, N=50) over the 7-day follow up. Rescue medication use was lower in the active arm vs. placebo (6.3% vs. 20.0%, p=0.02); and PROMIS PF-20 showed greater improvements over 7 days (22.2 vs. 16.7 points, p=0.05). The most common adverse event was hypertension (14.2%) with no significant difference between arms. Per protocol analyses were conducted to adjust for adherence on Day 1 for time to resolution of pain (Figure 1) and additional 24hr endpoints (Table 1).

Table 1. Key 24hr Endpoints (Per Protocol, n = 57)

	Active (n = 28)	Placebo (n = 29)	P value
Median time to resolution, hrs[1]	24	72	0.03
Change in 24hr PROMIS PF-20 score[2]	16.7	9.4	0.01
Physician-assessed moderate-to-severe joint tenderness 24hr[3]	28.0%	57.1%	0.02

[1]≥ 50% reduction in pain; K-M Est.; Subjects using rescue medication, discontinuing study drug, or missing pain scores censored [2]Consists of 20, 0-5-point questions; higher scores indicate better function [3]LIKERT: 0 (no pain), 1 (pain), 2 (wincing), 3 (wincing and withdrawal)



[1]Resolution is defined as at least a 50% reduction in pain; Kaplan-Meier Estimates; Subjects who use rescue pain medication, discontinue use of study drug, or otherwise have missing pain score data were censored at the date of the latest valid NRS pain score; Log-rank test for homogeneity between treatment K-M curves.

Figure 1. Time to resolution of pain[1] (per protocol population, n = 57)

Conclusion: Transdermal $NaHCO_3$ reduced the pain intensity and duration of an acute gout flare with higher overall response rates, faster time to resolution, improvements in physical function and a reduction in rescue medication use. The lack of adverse events makes this topical a promising therapeutic choice; especially during debilitating acute gout flares in patients with concomitant comorbidities.

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OP0171

A RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, MULTICENTER, STUDY OF METHOTREXATE COMBINED WITH PEGLOTICASE IN PATIENTS WITH UNCONTROLLED GOUT

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Background: Patients (pts) with gout refractory to oral urate-lowering therapy (ULT) have few treatment options. Pegloticase (pegylated uricase) lowers serum uric acid (sUA) in these pts,[1] but response rates are limited by anti-drug antibodies (ADAs), which decrease urate-lowering efficacy and increase infusion reaction (IR) risk.[2] Because methotrexate (MTX) is commonly used in RA