The Safety of IMC-1 in Patients With Fibromyalgia: Phase 2a Study Results

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INTRODUCTION

- Fibromyalgia (FM) is a chronic disorder characterized by widespread pain, fatigue, and cognitive impairment[1]
- Patients often experience inadequate relief with approved FM treatments, and many discontinue or switch treatments because of tolerability issues[2]
- It has been hypothesized that the reactivation of viral infections, such as herpes simplex virus type 1 (HSV-1), may contribute to the symptoms associated with FM and that drugs that suppress replication and/or reactivation of tissue-resident herpes virus could provide symptom relief[3]
- An oral, fixed dose combination of famciclovir and celecoxib (IMC-1) demonstrated greater tolerability and significantly greater pain reduction compared with placebo in a Phase 2a proof of concept trial (NCT01850420)[3]
- Given the considerable challenges of treating FM, there is a clear need for effective medications with better tolerability profiles to manage its symptoms

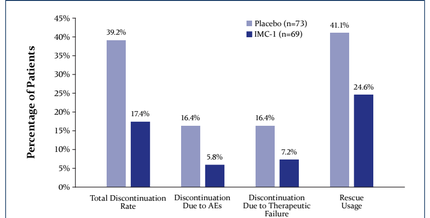
OBJECTIVE

- To evaluate the safety and tolerability of IMC-1 compared with placebo in patients with FM

RESULTS

- A total of 143 patients from 12 US sites were enrolled in the study and randomized to 16 weeks of treatment with IMC-1 (n=69) or placebo (n=74)
  - One patient randomized to the placebo group withdrew consent after randomization but prior to taking any study drug and was excluded from the analysis populations
- Baseline demographic and clinical characteristics were similar between treatment groups; most patients were Caucasian (95.8%) and female (93.7%) with a mean age of approximately 49 years
  - Patients in the placebo group had mean baseline NRS 24-hour recall scores of 7.1 compared to 6.5 for patients randomized to IMC-1 treatment; mean baseline FIQ-R 7-day recall pain scores were 6.8 in the placebo group and 6.5 in the IMC-1 group
- More patients in the placebo-treated group discontinued treatment prior to study completion compared with the IMC-1 treatment group (**Figure 1**)
- Discontinuation rates due to AEs in the placebo group were nearly 3-fold higher than the IMC-1 group (P=.012), and the rate of tramadol rescue medication usage for acute pain exacerbations was significantly lower in the IMC-1 group than in the placebo group (P=.037) (**Figure 1**)

Figure 1. Discontinuation Rates and Rescue Medication Usage

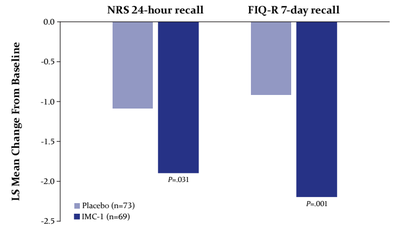


AEs, adverse events.

Efficacy Outcomes

- Patients treated with IMC-1 reported significantly greater reductions in pain versus placebo, as measured by mean change from baseline to week 16 in NRS 24-hour recall scores (-1.1 vs -1.9) (**Figure 2**)
- Similarly, significant improvement versus placebo was noted in FIQ-R 7-day recall scores in patients receiving IMC-1 treatment (-0.9 vs -2.2) (**Figure 2**)
- IMC-1 also exhibited consistent improvement versus placebo across several FM efficacy treatment outcomes, including 50% pain reduction responder analyses, functional assessments, fatigue scores, and global health status

Figure 2: Mean Change from Baseline in NRS and FIQ-R Pain Recall Scores at 16 Weeks



FIQ-R, Revised Fibromyalgia Impact Questionnaire; LS, least squares; NRS, numerical rating scale.

Treatment Emergent Adverse Events

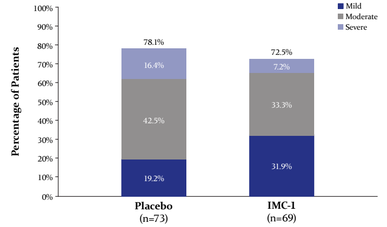
- TEAEs were reported by 72.5% of patients treated with IMC-1 and 78.1% of placebo-treated patients; overall, reported TEAEs were less severe in the IMC-1 group than the placebo group (**Table 1, Figure 3**)
- The most common TEAEs by organ class among both treatment groups were gastrointestinal disorders (35.9%), infections (24.6%), and nervous system disorders (20.4%)
- The most commonly reported TEAEs are summarized in **Table 1**
- No single AE caused discontinuation in multiple patients receiving IMC-1
- No deaths were reported; serious AEs were reported in 1 placebo-treated patient (breast cancer [unrelated]) and 2 IMC-1 treated patients (cellulitis [unrelated], acute myocardial infarction [possibly related])

Table 1. Treatment Emergent Adverse Event Summary

Adverse events	Placebo (n=73)	IMC-1 (n=69)
At least one TEAE, n (%)	57 (78.1)	50 (72.5)
>4% in either treatment group, n (%)		
Headache	10 (13.7)	8 (11.6)
Nausea	13 (17.8)	3 (4.3)
Diarrhea	9 (12.3)	3 (4.3)
Urinary tract infection	4 (5.5)	6 (8.7)
Vomiting	5 (6.8)	2 (2.9)
Constipation	6 (8.2)	0 (0.0)
Pyrexia	3 (4.1)	3 (4.3)

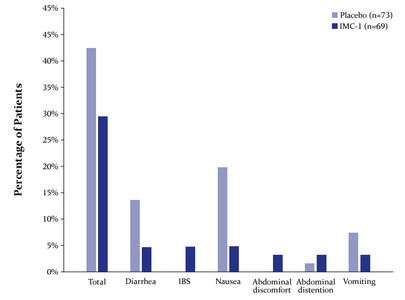
TEAE, treatment emergent adverse event.

Figure 3. Incidence of Any Treatment Emergent Adverse Events by Severity



- Interestingly, despite the celecoxib component of IMC-1, gastrointestinal TEAEs were reported less frequently in the IMC-1 group (29.0%) than the placebo group (42.5%) (**Figure 4**)

Figure 4. Gastrointestinal Treatment Emergent Adverse Events[a]



[a]Gastrointestinal TEAEs shown include events that occurred in ≥2% of the IMC-1 treatment group.
IBS, irritable bowel syndrome; TEAE, treatment emergent adverse event.

- A slightly higher frequency of TEAEs related to elevated hepatic enzymes was observed for IMC-1 versus placebo (lactate dehydrogenase [LDH] increased: 5.8% vs 1.4%; gamma glutamyl transpeptidase [GGT] increased: 2.9% vs 0), an unsurprising finding given celecoxib's known safety profile
- No clinically meaningful changes on hematology or chemistry parameters were noted in either treatment group
- A small increase from baseline in mean resting systolic blood pressure was noted in the IMC-1 treatment group compared with the placebo group (2.9 vs -2.4 mmHg)
  - Mean increases in weight (0.74 vs 0.27 kg) and body mass index (BMI) (0.28 vs 0.09 kg/m^2) were also slightly higher in the IMC-1 treatment group versus placebo

CONCLUSIONS

- IMC-1 exhibited an encouraging safety profile, as AEs occurred at a lower rate and were less severe in the IMC-1 treatment group compared with placebo
- As shown in Figure 1, the discontinuation rate due to AEs was nearly 3-fold higher in patients receiving placebo compared with patients receiving IMC-1, suggesting that treatment with IMC-1 was well-tolerated
- In this study, IMC-1 demonstrated significant reductions in pain, fatigue, and other symptoms in patients with FM
- These results suggest that IMC-1 may offer a promising and well-tolerated treatment option to relieve pain and other symptoms in patients with FM

REFERENCES

1. Clauw DJ. Fibromyalgia: a clinical review. *JAMA*. 2014;311(15):1547-1555.
2. Liu Y, Qian C, Yang M. Treatment Patterns Associated with ACR-Recommended Medications in the Management of Fibromyalgia in the United States. *J Manag Care Spec Pharm*. 2016;22(3):263-271.
3. Pridgen WL, Duffy C, Gendreau JF, Gendreau RM. A famciclovir + celecoxib combination treatment is safe and efficacious in the treatment of fibromyalgia. *J Pain Res*. 2017;10:451–460.

METHODS

Study Design and Patients

- A randomized, double-blind, placebo-controlled Phase 2a trial (NCT01850420) evaluated the safety and efficacy of IMC-1 for the treatment of adults (18–70 years) with a primary diagnosis of FM
  - Patients with baseline 24-hour recall average pain intensity scores between 4 and 9 on an 11-point numerical rating scale (NRS) were eligible for study enrollment
- Participants were randomized 1:1 to receive 16 weeks of treatment with IMC-1 or matching placebo
- Minimal use of acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) was permitted for minor pain, and if those agents were inadequate, tramadol could be prescribed as rescue therapy for acute pain exacerbations
- The primary efficacy outcome was mean change from baseline in FM pain assessed with a 24-hour recall, 11-point NRS pain scale, as well as a 7-day recall average pain score measured on the Revised Fibromyalgia Impact Questionnaire (FIQ-R)
  - Data were analyzed in the intent-to-treat population (ITT) using a mixed-effect model repeated measures (MMRM) approach with last observation carried forward (LOCF) and baseline observation carried forward (BOCF) imputation
- The percentage of Patient's Global Impression of Change (PGIC) responders, defined as patients who rated themselves "very much improved" or "much improved" (ie, scores of 1 or 2 on the 7-point scale), FIQ-R scores, and pain reduction responder analyses were examined as secondary outcomes
- Patient-Reported Outcomes Measurement Information System (PROMIS) fatigue scores and Multidimensional Fatigue Inventory (MFI) scores were examined as exploratory efficacy outcomes
- Safety assessments included vital signs, adverse events (AE), and clinical laboratory monitoring to analyze the outcomes of treatment emergent AEs (TEAEs), discontinuation due to AEs, AE severity, rescue medication usage, and laboratory parameters
  - The safety population consisted of all randomized participants who took at least one dose of study drug; safety data were analyzed descriptively

Disclosures

William Pridgen is a founder and member of the board of directors of Virios Therapeutics. Carol Duffy has served as a consultant for Virios Therapeutics and the University of Alabama, Department of Biological Sciences and has received financial research support from Innovative Med Concepts (now Virios Therapeutics) in the form of two Sponsored Research Agreements. Judy F. Gendreau has served as a consultant for Tonix Pharmaceuticals, Dare Bioscience and Virios Therapeutics. R. Michael Gendreau has served as a consultant for Tonix Pharmaceuticals, Teva Pharmaceuticals, Swing Therapeutics, Bionomics Limited, Dare Bioscience and is an employee of Virios Therapeutics.

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