

**Safety and Tolerance of Crofelemer 125 mg Twice Daily in the Treatment of Noninfectious Diarrhea in HIV-Positive Patients: Results of a Phase 3, 48-Week Open-Label Study**

Trevor N. Hawkins, MD; Roger D. MacArthur, MD; Stephen J. Brown, MD; Patrick G. Clay, PharmD; Lawrence Waldman, MD; Andrew C. Barrett, PhD; Encho Borety, PhD; Craig Paterson, MD; and William P. Forbes, PharmD

**Introduction**

Crofelemer (Fulyzaq™, Salix Pharmaceuticals, Inc., Raleigh, NC, USA) is a minimally absorbed, first-in-class, botanically derived drug indicated for the symptomatic relief of noninfectious diarrhea in adults with HIV. The ADVENT trial was a phase 3, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of crofelemer 125 mg twice daily in patients with HIV who were receiving ART and had noninfectious diarrhea. The primary objective was to determine the proportion of patients achieving ≤2 watery stools per week for ≥2 of the first 4 weeks of treatment. Secondary objectives included assessment of the proportion of patients achieving stool consistency and clinical response.

**Methods**

**Study Design and Population**

The ADVENT trial was a 48-week open-label study of crofelemer 125 mg twice daily for up to 46 weeks. The study included all patients who were receiving ART with a baseline HIV viral load of >400 copies/mL and at least 1 episode of noninfectious diarrhea in the previous 6 months. Patients were randomized to crofelemer 125 mg twice daily or placebo for 24 weeks, followed by a 24-week open-label extension study. The safety population included all patients who received ≥1 dose of study medication.

**Efficacy**

**Safety**

In a phase 3, double-blind, placebo-controlled trial (ADVENT), crofelemer 125 mg twice daily significantly reduced diarrhea in patients with HIV receiving ART compared with placebo, and the safety profile was comparable to placebo for up to 24 weeks.

**Results**

The ADVENT trial included 251 patients; 250 were included in the safety population. The median days (range) of exposure to study drug was 335 (7-366) days, with 31.2% and 68.8% of patients completing 9 and 12 months, respectively. Efficacy analyses were performed on the intent-to-treat (ITT) and safety populations, with results from the ITT population reported in this article.

**Conclusions**

Crofelemer 125 mg twice daily was well tolerated with a low incidence of AEs in HIV-seropositive patients with noninfectious diarrhea receiving ART that is consistent with the minimal and systemic absorption of crofelemer. This study demonstrates the absence of an important adverse effect on HIV status, supportive of adherence to ART regimens and continued ART efficacy.

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