**INTRODUCTION**

- FXR agonists have previously demonstrated dose-related pruritus and unfavorable lipid effects in NASH patients.
- TERN-101 is a potent, non-steroidal FXR agonist with enhanced liver distribution, being developed for the treatment of NASH.
- In the Phase 2a LIFT study, TERN-101 5 mg, 10 mg, and 15 mg vs placebo administered for 12 weeks to NASH patients was overall safe and well-tolerated with significant reductions in corrected T1 (cT1) and decreases in alanine aminotransferase (ALT) and magnetic resonance imaging proton density fat fraction (MRI-PDFF).

**OBJECTIVE**

- To report detailed lipid and pruritus from the LIFT study.

**METHODS**

- LIFT was a randomized, double-blind, placebo-controlled Phase 2a study (NCT04328077) evaluating 5 mg, 10 mg, and 15 mg TERN-101 administered for 12 weeks in 100 adults with NASH (Figure 1).
- LDL and HDL were assessed at baseline and every 4 weeks.
- Percent change from baseline in LDL and HDL over time was analyzed using an analysis of covariance (ANCOVA) model with percent change from baseline as the dependent variable including treatment group as a fixed effect and baseline as a covariate. Post-hoc analyses of degree of cholesterol change from baseline included:
  - LDL increase by threshold of ≥25 mg/dL at Week 12
  - HDL decrease by threshold of ≥10 mg/dL at Week 12
- Pruritus was graded per common terminology criteria for adverse events (CTCAE):
  - Grade 0: Mild or localized; topical intervention indicated.
  - Grade 1: Widespread and intermittent; skin changes from scratching (e.g., edema, papulation, excoriation, lichenification, pruritus); oral intervention indicated; limiting instrumental activities of daily living (iDLD).
  - Grade 2: Widespread and constant; limiting self-care, ADL, or sleep; systemic corticosteroid or immunosuppressive therapy indicated.

**RESULTS**

- TERN-101 was generally well-tolerated with minimal pruritus and no difference from placebo in LDL or HDL change from baseline in the 5 mg and 10 mg dose groups.
- TERN-101 doses lower than 15 mg did not result in a clinically meaningful or sustained change from baseline in LDL or HDL through 12 weeks of treatment.
  - LDL and HDL mean changes, and proportion of patients with lipid changes by specified thresholds, were similar for 5 and 10 mg TERN-101 and placebo at Week 12.
- Pruritus reported with TERN-101 was generally mild and transient.
- Pruritus AEs were not TERN-101 dose-dependent and did not lead to treatment discontinuation.
- No widespread or constant pruritus (Grade 3) occurred with TERN-101.
- TERN-101 has a favorable, differentiated safety and tolerability profile at potentially efficacious dose levels.

**OVERALL SAFETY**

- Overall AE incidences were generally similar across all treatment groups.
- There were no treatment discontinuations due to any AE, including pruritus, in any treatment group or treatment related serious AEs.
- Common treatment emergent AEs (TEAEs) other than pruritus were balanced across TERN-101 groups and placebo.

**LIPID PROFILE**

- No difference in LDL and HDL percent change from baseline was observed for 5 mg and 10 mg TERN-101 vs placebo at any timepoint.
- In the TERN-101 15 mg group, LDL (Figure 2A) and HDL changes (Figure 2B) were significantly different from placebo.
- Lipid-lowering therapy was not initiated or changed for any patients during the treatment period.
- LDL decreases of ≥25 mg/dL, as Week 12 were similar across TERN-101 treatment groups and placebo (Figure 2C).
- Less than 10% patients in TERN-101 5 mg or placebo had decreases from baseline in HDL of ≥10 mg/dL (Figure 2C).

**PRURITUS**

- Pruritus AEs were balanced across TERN-101 groups.
- 14.9% overall across all dose groups (Table 3).
- Pruritus onset ranged from Day 2 to Day 73 and resolved with ongoing TERN-101 treatment for 6 of 11 patients.
- There were no Grade 3 pruritus events or study drug discontinuation due to pruritus in any treatment group.
- Grade 2 pruritus occurred in only three patients:
  - Two patients in the TERN-101 10 mg group (generalized pruritus)
  - One patient in the TERN-101 15 mg group (pruritus localized to bilateral forearms)

**REFERENCES**


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**CONTACTS AND DISCLOSURES**

- TERN-101 is an investigational drug being developed by Terns Pharmaceuticals, which provided funding for the study as well as the post-study preparation services.

**Favorable lipid and pruritus profile of liver-distributed farnesoid X receptor (FXR) agonist TERN-101 at clinically efficacious doses in nonalcoholic steatohepatitis (NASH) phase 2a lift study**

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