Poster No. SAT106

TERN-101, A FARNESOID X RECEPTOR (FXR) AGONIST, DEMONSTRATED SIMILAR SAFETY AND EFFICACY IN NONALCOHOLIC STEATOHEPATITIS (NASH) PATIENTS WITH CORONAVIRUS DISEASE OF 2019 (COVID-19) EXPOSURE COMPARED TO THOSE WITH NO COVID-19 EXPOSURE IN PHASE 2A LIFT STUDY

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SCAN ME!

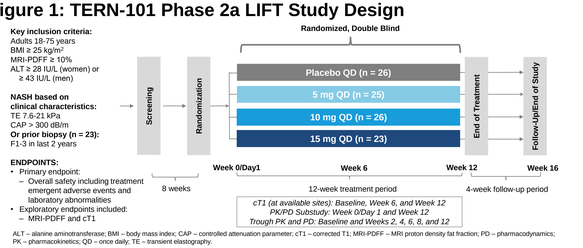
KEY TAKEHOME MESSAGE

- COVID-19 exposure did not impact the overall safety and efficacy results of TERN-101 in a 12-week, Phase 2a study in patients with presumed NASH.

1 • INTRODUCTION

- TERN-101 is a potent, non-steroidal FXR agonist with enhanced liver distribution, being developed for the treatment of NASH.
- The Phase 2a LIFT study assessed multiple doses of TERN-101 vs placebo for 12 weeks in non-cirrhotic patients with NASH (Figure 1).
- The LIFT study showed TERN-101 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).[1]
- The LIFT study was conducted entirely during the COVID-19 pandemic, thereby allowing analyses of TERN-101 administered in the setting of COVID transmission.
- We evaluated overall safety and key efficacy parameters in NASH patients with COVID-19 exposure during participation in the LIFT study.

Figure 1: TERN-101 Phase 2a LIFT Study Design



ALT – alanine aminotransferase; BMI – body mass index; CAP – controlled attenuation parameter, cT1 – corrected T1; MRI-PDFF – MRI proton density fat fraction; PD – pharmacodynamics; PK – pharmacokinetics; QD – once daily; TE – transient elastography.

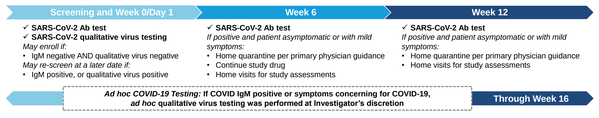
2 • OBJECTIVE

- To explore any potential impact of COVID-19 exposure on safety or efficacy of TERN-101 in Phase 2a LIFT study.

3 • METHODS

- LIFT was a randomized, double-blind, placebo-controlled Phase 2a study (NCT04328077) which was conducted entirely in the U.S. between June 2020 and May 2021 and evaluated 5 mg, 10 mg, and 15 mg TERN-101 administered for 12 weeks in 100 adults with NASH (Figure 1).
- All study participants were randomized between July 2020 and January 2021, prior to the availability of COVID-19 vaccinations in the U.S.
- COVID-19 testing was performed at Screening and at Weeks 0 (Day 1), 6, and 12 during the study. Antibody testing was required, with *ad hoc* antibody and/or PCR testing in the event of COVID-19 symptoms (Figure 2).
- COVID-19 vaccination was permitted and was recorded as a concomitant medication (COVID-19 vaccines became available in the U.S. after LIFT enrollment was completed and while study medication dosing was ongoing).
- COVID-19 exposure was defined as:
  - COVID-19 infection reported as an adverse event (AE), or
  - Detectable COVID-19 antibodies during the study (at Week 0/Day 1 or later)

Figure 2: Screening and On-Study COVID-19 Testing



LabConnect initially utilized National Jewish Health Laboratory to conduct COVID-19 IgG and IgM using EDI assay under EUA. EUA revoked and switched to Abbott assay when ~20% of antibody tests were outstanding (~ end February 2021). 84 patients had samples available to re-test (variety of timepoints). Of the samples that were re-assayed, 16 (6%) showed discrepant results in 10 patients. Ab – antibody; COVID-19 – coronavirus disease of 2019; EUA – Emergency Use Authorization, IgM – immunoglobulin M; SARS-COV-2 – severe acute respiratory syndrome coronavirus 2.

4 • RESULTS

OVERVIEW OF COVID-19 TESTING RESULTS AND TOTAL CASES OF COVID-19 EXPOSURE

- ***COVID-19 Polymerase Chain Reaction (PCR) testing***
  - 7 out of 446 potential participants screened for the study had a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) PCR test at screening and were excluded from the study.
  - No positive SARS-CoV-2 PCR test results were reported through on-study testing.
- ***COVID-19 Antibody (Ab) testing***
  - 20 patients with positive COVID-19 antibody results (EDI or Abbott or local lab) from Week 0 through Week 12.
    - 4 of the patients developed detectable antibodies after COVID-19 vaccinations.
- A total of 24 COVID-19 exposure cases were identified during the study: 20 patients with COVID-19 antibody at Week 0 or later and 4 additional patients with COVID-19 AEs.
- The demographics and baseline characteristics of patients with or without identified COVID-19 exposures are shown in Table 1.

Table 1: Patient Demographics and Baseline Characteristics

Patient Demographics and Baseline Characteristics	No Identified COVID-19 Exposure* N = 76				Identified COVID-19 Exposure† N = 24			
		TERN-101				TERN-101		
	Placebo (n = 21)	5 mg (n = 17)	10 mg (n = 21)	15 mg (n = 17)	Placebo (n = 5)	5 mg (n = 8)	10 mg (n = 5)	15 mg (n = 6)
Age, mean (SD) [years]	49.4 (11.8)	49.1 (12.0)	53.4 (13.1)	51.8 (10.5)	54.6 (5.4)	45.9 (13.4)	48.4 (16.9)	51.2 (6.4)
Sex, n (%)								
Male	10 (47.6)	6 (35.3)	7 (33.3)	3 (17.6)	0	4 (50.0)	2 (40.0)	3 (50.0)
Race, n (%)								
White	18 (85.7)	16 (94.1)	17 (81.0)	16 (94.1)	3 (60.0)	7 (87.5)	4 (80.0)	5 (83.3)
Ethnicity, n (%)								
Hispanic or Latino	15 (71.4)	10 (58.8)	12 (57.1)	14 (82.4)	5 (100.0)	7 (87.5)	4 (80.0)	3 (50.0)
BMI, mean (SD) [kg/m²]	35.7 (5.5)	37.3 (6.2)	35.7 (6.0)	36.5 (4.9)	39.8 (3.9)	37.1 (7.3)	39.0 (9.3)	35.3 (4.5)
ALT, mean (SD) [IU/L]	56.9 (25.0)	57.2 (15.7)	60.9 (28.1)	61.8 (27.9)	49.6 (17.7)	54.3 (18.3)	60.5 (36.5)	38.7 (10.7)
MRI-PDFF, mean (SD) [%]	22.1 (7.5)	21.8 (9.5)	20.4 (7.8)	22.0 (7.1)	18.5 (7.9)	19.6 (4.7)	18.6 (2.4)	25.1 (12.1)
cT1, mean (SD) [msec]‡	908.0 (92.8)	928.9 (68.0)	930.1 (153.4)	978.1 (190.8)	913.0 (94.6)	918.5 (92.5)	989.5 (95.0)	957.7 (74.9)

*Patients without a positive COVID test at Weeks 0, 6, or 12 and no AE of COVID.
†Patients with a positive COVID test at Weeks 0, 6, or 12 or AE of COVID.
‡cT1 conducted at sites with this capability.
AE – adverse event; ALT – alanine aminotransferase; BMI – body mass index; COVID – coronavirus disease; cT1 – corrected T1; MRI-PDFF – MRI proton density fat fraction; SD – standard deviation.

ADVERSE EVENTS

- Of 100 enrolled and treated patients, 96% completed the LIFT study with no discontinuations due to AEs and no deaths.
  - AEs occurred in 38.5% of the placebo and 56.8% of the TERN-101 groups (Table 2).
- COVID-19 infection was reported for 7 patients (7%) (Table 2):
  - 6 who received TERN-101 and had mild to moderate AEs (Grade 1 or 2).
  - 1 placebo patient who had a severe/serious AE that eventually resolved.
- Similar rates of AEs were reported between patients without COVID-19 exposure and with COVID-19 exposure.

Table 2: Overall Summary of Adverse Events

Patient incidence AEs by category, n (%)	Placebo (n = 26)	TERN-101 5 mg (n = 25)	TERN-101 10 mg (n = 26)	TERN-101 15 mg (n = 23)
Any AE, all CTCAE grades	10 (38.5%)	13 (52.0%)	14 (53.8%)	15 (65.2%)
CTCAE Grade 3 or higher AEs	1 (3.8%)	0	0	1 (4.3%)
Serious AE	1 (3.8%)	0	0	1 (4.3%)
AE leading to discontinuation of study drug or study	0	0	0	0
Any COVID-19 AE, any grade	1 (3.8%)	2 (8.0%)	1 (3.8%)	3 (13.0%)
Grade 1	0	1 (4.0%)	0	2 (8.7%)
Grade 2	0	1 (4.0%)	1 (3.8%)	1 (4.3%)
Grade 3	1 (3.8%)	0	0	0
Serious AE	1 (3.8%)	0	0	0

AEs reported refer to treatment emergent AEs, defined as any AE with a start date on or after the date of first administration of study drug through 30 days after the last administration of study drug or through the Follow-Up Period (Week 16). Severity of adverse events was graded according to CTCAE version 5.
AE – adverse event; CTCAE – common terminology criteria for adverse events.

RESPONSES TO THERAPY

- Relative changes in MRI-PDFF (Figure 3A) and changes in cT1 (Figure 3B) at Week 12 in patients with COVID-19 exposure were generally similar to those in patients without COVID-19 exposure.

Figure 3A: MRI-PDFF Relative Changes at Week 12

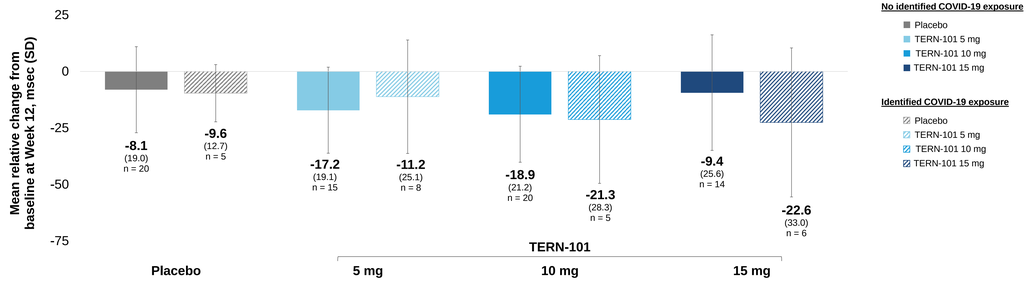
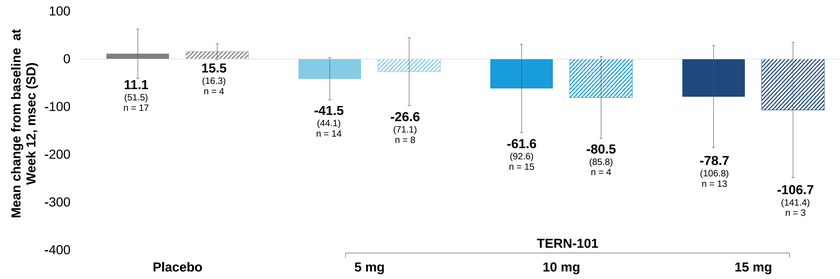


Figure 3B: cT1 Changes at Week 12



COVID-19 - coronavirus disease of 2019; cT1 – corrected T1; MRI-PDFF – MRI proton density fat fraction; SD – standard deviation.

5 • CONCLUSIONS

- Patient recruitment and retention in the LIFT study was feasible during the COVID-19 pandemic with successful implementation of COVID-19 testing.
- The TERN-101 safety profile and responses in the key efficacy imaging endpoints including MRI-PDFF and cT1 were overall similar between the patients with identified COVID-19 exposure and those without.
- Utilization of COVID-19 testing supported successful study conduct despite the COVID-19 pandemic without an obvious impact on the study results (NCT04328077).

6 • CONTACTS AND DISCLOSURES

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

7 • REFERENCE

1) Loomba R et al. Liver-distributed FXR Agonist TERN-101 demonstrates favorable safety and efficacy profile in NASH Phase 2a LIFT study. Abstract presented at: The Liver Meeting® of the American Association for the Study of Liver Diseases; November 12-15, 2021.

8 • ACKNOWLEDGEMENTS

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