No Effect of Food or Proton Pump Inhibitor on the Pharmacokinetics of TERN-601, An Oral Small Molecule GLP-1 Receptor Agonist

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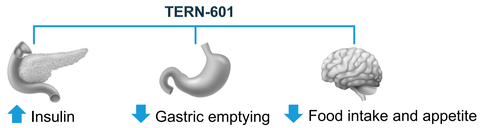
1 INTRODUCTION

- TERN-601 is an oral, small molecule GLP-1 receptor (GLP-1R) agonist
- TERN-601 suppresses food intake, slows gastric emptying, and reduces blood glucose in mice expressing human GLP-1R[1]
- In a first-in-human study, TERN-601 was well-tolerated over 28 days of dosing and achieved weight loss of up to 5.5% (Abstract #307-OR[2])
- This study was conducted to support dosing recommendations and concomitant medication allowances in the ongoing 12-week Ph 2 study (NCT06854952)

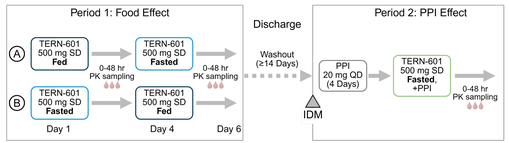


2 STUDY OBJECTIVES

- **Primary**:
  - To evaluate the effect of food on TERN-601 pharmacokinetics (PK)
  - To evaluate the effect of a representative proton pump inhibitor (PPI) on TERN-601 PK
- **Secondary:**
  - To evaluate the safety and tolerability of TERN-601 in the fed and fasted state
  - To evaluate the safety and tolerability of TERN-601 when co-administered with a PPI

3 METHODS / STUDY DESIGN

- Population: Otherwise healthy adults with BMI ≥25 kg/m^2 to <40 kg/m^2 and HbA1c <6.5%
- N = 10 randomized 1:1 to Sequence A or B
- Fed state: high-fat meal (800-1000 kcal; ~50% from fat)
- TERN-601: 500 mg, immediate release
- PPI (proton pump inhibitor): rabeprazole, 20 mg QD
- Interim decision meeting (IDM) held to review food effect PK data to determine if TERN-601 should be dosed fed or fasted with PPI



- PK parameters estimated by noncompartmental analysis (WinNonlin)
- Ratios of geometric least squares means (GLSMs) and 90% confidence intervals (CIs) were derived for AUC and C_{max} for the fed vs fasted treatments and w/PPI vs alone treatments

4 RESULTS

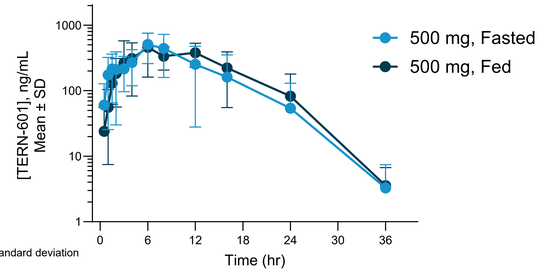
Demographics and Baseline Characteristics

- Aged 25 to 54 yo
- 70% male
- 90% White, 10% Black or African American
- Baseline BMI 25 to 37 kg/m^2

Safety

- No treatment-emergent adverse events were reported
- No clinically meaningful changes in laboratory values, vital signs, or ECGs

No Effect of Food on TERN-601 Exposure

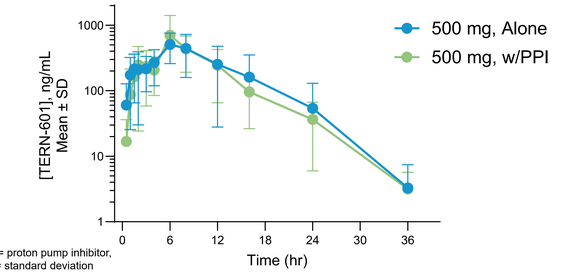


SD = standard deviation

PK Parameter	TERN-601 Fasted (N=10)	TERN-601 Fed (N=10)	%GLSMR (90% CI)
C_{max}, ng/mL	652 (35.8)	567 (50.2)	82.0 (57.0, 118)
AUC_{last}, hr.ng/mL	5500 (50.2)	6180 (40.8)	118 (100, 139)
AUC_{inf}, hr.ng/mL	5520 (50.1)	6190 (40.7)	118 (100, 139)
$AUC_{\%exp}$ (%)	0.32 (77.2)	0.22 (64.3)	--
T_{max}, hr	6.00 (1.00, 16.00)	6.00 (3.00, 12.00)	--
$t_{1/2}$, hr	3.05 (2.30, 8.35)	3.23 (2.17, 3.98)	--

- No change in AUC when TERN-601 was dosed in fed vs. fasted state
  - Slight decrease in variability (%CV)
- Slight decrease in C_{max} (18%) that is not clinically meaningful
- No change in T_{max} or $t_{1/2}$

No Effect of Gastric Acid Reducing Agents on TERN-601 Exposure



PPI = proton pump inhibitor, SD = standard deviation

PK Parameter	TERN-601 Alone (N=10)	TERN-601 w/PPI (N=10)	%GLSMR (90% CI)
C_{max}, ng/mL	652 (35.8)	785 (82.9)	99.8 (69.0, 144)
AUC_{last}, hr.ng/mL	5500 (50.2)	5250 (58.0)	89.3 (72.0, 111)
AUC_{inf}, hr.ng/mL	5520 (50.1)	5270 (57.9)	89.5 (72.2, 111)
$AUC_{\%exp}$ (%)	0.32 (77.2)	0.49 (76.5)	--
T_{max}, hr	6.00 (1.00, 16.00)	6.00 (2.00, 8.00)	--
$t_{1/2}$, hr	3.05 (2.30, 8.35)	3.89 (3.28, 7.51)	--

- No change in AUC or C_{max} when TERN-601 is dosed with PPI vs alone
- No change in T_{max} or $t_{1/2}$

Tables: Values are reported to 3 significant figures; Data are expressed as mean (%CV) with the exception of T_{max} and $t_{1/2}$ which are expressed as median (min, max); CI = confidence interval; %CV = percent coefficient of variability; %GLSMR = percent geometric least squares mean ratio; C_{max} = maximum concentration; AUC_{last} = area under the concentration time curve from time 0 to last observed concentration; AUC_{inf} = area under the concentration time curve from time 0 extrapolated to infinity; $AUC_{\%exp}$ = percent of AUC_{inf} extrapolated beyond last observed concentration; T_{max} = time of maximum concentration; $t_{1/2}$ = terminal elimination half-life

Food and PPI Effect GLSMR (Fold-change)

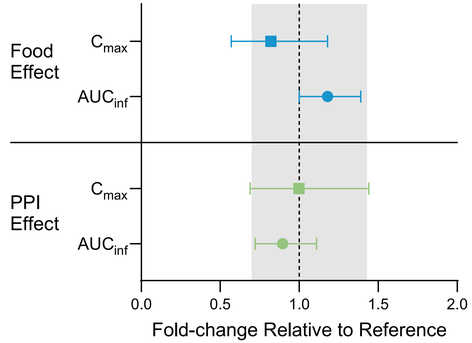


Figure: Forest plot of GLSM ratios for C_{max} and AUC_{inf} when comparing TERN-601 dosed with food vs fasted (food effect) and dosing TERN-601 with a PPI vs alone in the fasted state (PPI Effect). Gray shaded region represents 70-143% bounds.

5 CONCLUSIONS

- TERN-601 was well-tolerated
- TERN-601 can be dosed without regard to food
- TERN-601 can be co-administered with gastric acid reducing agents including proton pump inhibitors (PPIs), histamine-2 receptor antagonists (H2RAs), and/or antacids
- **Ongoing 12-week Ph 2 study (NCT06854952) has no restrictions on dosing with food or gastric acid reducing agents**

REFERENCES

1. Jones C, et al. *Diabetes*. 2023;72(Suppl 1):767-P.
2. Nelson C, et al. *Diabetes*. 2025;74(Suppl 1):307-OR.

ACKNOWLEDGEMENTS

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DISCLOSURES

- This study was funded by Terns Pharmaceuticals.
- All authors are employees/consultants of Terns Pharmaceuticals and may be shareholders.