An *In Vitro* Recovery Study of Sodium Phenylbutyrate and Taurursodiol From 3 Types of Dosing Containers and Various Percutaneous Endoscopic Gastrostomy Feeding Tubes

Poster #124

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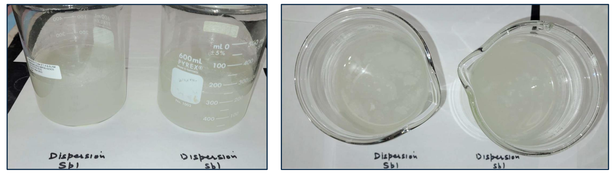
BACKGROUND

- Sodium phenylbutyrate and taurursodiol (PB&TURSO) is approved to treat amyotrophic lateral sclerosis (ALS) in the United States[1] and approved with conditions in Canada for the treatment of ALS[2]
- PB&TURSO is considered an oral suspension, not an oral solution[1]
  - According to the United States Pharmacopeia Expert Committee on Nomenclature and Labeling Nomenclature Guidelines, suspensions are defined as liquid preparations containing drug substance(s) and consist of solid particles dispersed throughout a liquid phase in which the particles are present in excess of the solubility[3]
- PB is a white or yellow powder that is freely soluble in water, and TURSO is an ambiphilic bile acid, a white microcrystalline powder that is sparingly soluble in water[1]
- PB&TURSO combination is a white to yellow powder for oral suspension that consists of fine to large granules[1]
- When prepared for administration after stirring vigorously in water (as prepared according to the recommended instructions), PB&TURSO may appear cloudy and/or contain residue[1,4] (**Figure 1**)

FIGURE 1. PB&TURSO SUSPENSION



- The efficacy and safety of PB&TURSO combination were assessed in the CENTAUR clinical trial, a phase 2, multicenter trial in adults living with amyotrophic lateral sclerosis (ALS)[5]
- Trial participants (N=137) were randomized 2:1 to PB&TURSO (n=89) or matching placebo (n=48) administered once daily by mouth or via feeding tube for 3 weeks and then twice daily (1 packet in the morning and 1 packet in the evening), if well tolerated, for the 24-week randomized controlled phase[5]
  - Placebo was matched with PB&TURSO for appearance, taste and solubility
- For all participants, the study drug was stirred vigorously in 8 ounces (≈237 mL) of room temperature water; the mixture was either consumed orally or administered via feeding tube for participants with a gastrostomy or nasogastric tube within 1 hour of mixing[6]
- Twenty-eight CENTAUR participants were reported as using a feeding tube—16 participants (18%) receiving PB&TURSO and 12 participants (25%) receiving placebo[4,5]
- The adverse event profile was similar between PB&TURSO and placebo participants using a feeding tube in the trial[4]

OBJECTIVE

- To evaluate PB&TURSO oral suspension administration via different feeding tube and dosing container combinations as part of an *in vitro* recovery study

METHODS

Feeding Tubes and Dosing Containers

- Five types of percutaneous endoscopic gastrostomy (PEG) feeding tubes, also known as G tubes (manufactured by Avanos Medical, Inc.) (**Table 1**), and three types of dosing containers were tested (**Table 2**)
  - Several combinations of feeding tubes and dosing containers were used to evaluate PB&TURSO recovery via chromatography and were visually inspected (**Figure 2**)

TABLE 1. FEEDING TUBES TESTED

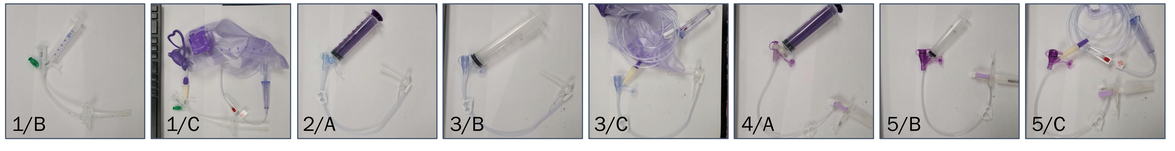
Feeding Tube	1	2	3	4	5
Description	One-piece PEG long G-Tube with balloon	Low-profile PEG G-Tube with balloon with right-angle, 12-inch ENFit extension set	Low-profile PEG G-Tube with balloon with right-angle, 12-inch catheter tip extension set	Low-profile PEG G-Tube with retention bolster with right-angle. 12-inch ENFit feeding extension set	Low-profile PEG G-Tube with retention bolster with right-angle. 12-inch catheter tip extension set
Material of construction	Medical-grade silicone	Medical-grade silicone	Medical-grade silicone	Medical-grade silicone	Medical-grade silicone
Tube size, Fr	14	12	12	14	14
Stoma length, cm	24	4	4	3	3

TABLE 2. DOSING CONTAINERS TESTED

Dosing Container	A	B	C
Description	ENFit tip syringe used as dosing container comes with feeding tube kit	50-mL Luer-Lok™ tip syringe (used as catheter tip)	Gravity feeding bag including ENFit connector, PVC, ABS, PP material
Material of construction	Medical-grade silicone	Medical-grade silicone	Medical-grade silicone
Volume, mL	35	50	1000

ABS, acrylonitrile butadiene styrene; PP, polypropylene; PVC, DEHP-free polyvinyl chloride.

FIGURE 2. COMBINATION OF FEEDING TUBES AND DOSING CONTAINERS USED FOR SAMPLE ADMINISTRATION



In Vitro Recovery Assay

- An *in vitro* recovery study was conducted using 1 packet of PB&TURSO for the morning dose and 1 packet of PB&TURSO for the evening dose (each packet mixed with 8 ounces [≈237 mL] of room temperature water)
  - Each feeding tube setup was flushed with 20 mL of water before and after dose administration
- Two samples for each combination of feeding tube and dosing container were prepared and assayed via high-performance liquid chromatography to determine the percentage of PB&TURSO at feeding tube exit
  - Room temperature water was used as dosing media
  - All samples were mixed for up to 20 minutes or when reconstitution was achieved
  - Each test set was dosed 2 times to represent the morning dose and the evening dose
- The % recovery of PB&TURSO at the feeding tube exit was calculated as follows:

$$\%\ \text{recovery} = \frac{\%\ \text{LC}_{\text{feeding tube}}}{\%\ \text{LC}_{\text{initial dispersion}}} \times 100$$

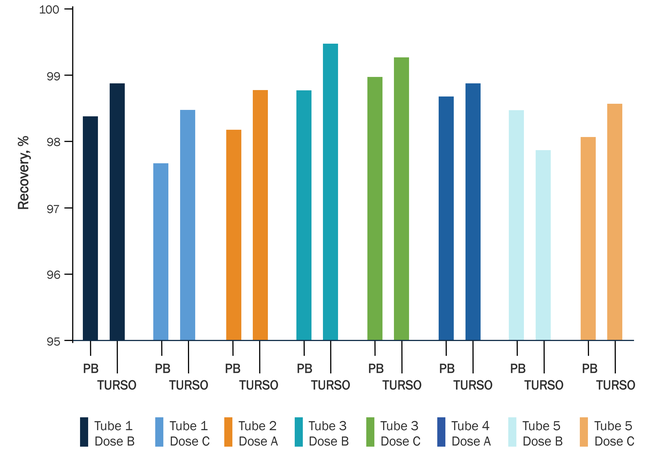
where:
LC = concentration of PB or TURSO in the solution
% LC feeding tube = % LC of PB or TURSO at feeding tube exit from assay sample solution
% LC initial dispersion = % LC of PB or TURSO from control sample solution

- Acceptance criterion for *in vitro* recovery was defined as within 90% to 110% recovery of PB&TURSO at the feeding tube exit relative to the control

RESULTS

- All combinations of feeding tubes and dosing containers described met defined acceptance criteria (**Figure 3**)

FIGURE 3. PB&TURSO FEEDING TUBE RECOVERY[a]



[a]Values displayed on this figure reflect mean % recovery
Dose, dosing container; tube, feeding tube. For more information about the feeding tubes and dosing containers tested, refer to table 1 and table 2, respectively.

- The feeding tubes and dosing containers used underwent visual examination, and no sedimentation, aggregation, adherence, build-up, or clogging were observed

CONCLUSION

In vitro data support that PB&TURSO can be used in a variety of PEG tube and dosing container combinations

Acknowledgments

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Disclosures

MM, SS, JL, and SC are full-time employees of and may have stock ownership in Amylyx Pharmaceuticals, Inc.

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