



# THRIVE-1: A multi-center, cross-sectional, observational study to assess the prevalence of choline deficiency in patients dependent on parenteral support

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Poster No: LBO52

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## Background

- Choline is a quaternary amine that is an essential dietary nutrient in humans<sup>1,2</sup>
- Choline deficiency can lead to hepatic injury, neuropsychological impairment, muscle damage, and thrombotic abnormalities<sup>3-6</sup>
- Choline is essential for patients with intestinal failure (IF) who are dependent on Parenteral Support (PS)
- Current PS formulations lack choline, affecting an estimated 40,000 long-term PS patients who are or may become deficient<sup>7</sup>
- Currently, there are no approved intravenous choline products for PS patients globally

## Methods

- THRIVE-1 was a prospective, multi-center, cross-sectional, observational study
- This study assessed the prevalence of choline deficiency and liver injury in male and female adolescents ( $\geq 12$  years of age) and adult patients ( $\geq 18$  years of age) with IF who are dependent on PS
  - PS dependence defined as at least 4 days/week on PS for 10 to 24 weeks (capped at 25%) and 24 weeks or longer
- Data collection occurred during a single clinic visit

## Results

- 78 patients enrolled; 75 completed and 3 withdrew the study
- Demographics:
  - 55% male, 92% White, 96% Not Hispanic or Latino
  - Mean age: 52 years (SD: 16.6)
  - Mean height: 167.59 cm (SD: 10.2)
  - Mean weight: 64.73 kg (SD: 13.5)
  - Mean BMI: 22.95 kg/m<sup>2</sup> (SD: 3.8)
- Parenteral Support (PS):
  - Mean duration: ~9 years (Range: 10 weeks to 2319 weeks)
  - Mean PS frequency: 6.6 days/week (SD: 0.95)
  - Received mixed lipids: 40% (31/78)
    - Fish oil based lipid: Omegaven
    - Plant based (soybean oil lipid, olive oil lipid): Clinolipid; Intralipid
    - Nutrilipid Mixed oil lipids (fish oil and plant based): SMOF
  - Received plant-based lipids: 49% (38/78)
- Patients had at least one of the following underlying conditions based on ESPEN Pathophysiological IF Classification:
  - Short Bowel Syndrome: 59% (46/78)
  - Mucosal Diseases: 46% (36/78)
  - Chronic Intestinal Dysmotility Disorders: 33% (26/78)
  - Mechanical Obstruction: 8% (6/78)
  - Intestinal Fistulae: 6% (5/78)
- 78% (61/78) were choline deficient
  - Choline deficiency was defined as plasma free choline concentration  $< 9.5$  nmol/mL
  - Mean plasma free choline concentration: 7.5 nmol/mL (SD: 3.9)
- 63% (38/60) of choline deficient participants had liver injury
  - Liver injury was defined as elevated liver tests [ $> 1.5 \times$  ULN; ALP, AST, ALT, GGT, direct bilirubin, total bilirubin] or steatosis [MRI-PDFF  $\geq 8\%$ ]

## Summary/Highlights

- The high prevalence of choline deficiency among patients with IF who are dependent on PS emphasizes the need for choline supplementation
- This patient population has an unmet need for IV choline that should be addressed
- Significant heterogeneity of liver injury was observed and warrants further investigation
- Protara is developing Choline Chloride for Injection, a phospholipid substrate replacement therapy, as a source of choline to potentially enhance health outcomes for long-term PS-dependent patients
- Protara intends to initiate a Phase 2b/3 safety and efficacy study of IV Choline Chloride in the first quarter of 2025

Table 1. Overview of Demographics, Baseline Characteristics

Characteristics	Enrolled Set (N = 78)
<b>Age (years)</b>	
Mean (SD)	51.9 (16.6)
<b>Age group, n (%)</b>	
12-<18	2 (2.6)
18-65	61 (78.2)
>65	15 (19.2)
<b>Sex, n (%)</b>	
Male	43 (55.1)
Female	35 (44.9)
<b>Race, n (%)</b>	
Asian	2 (2.6)
Black or African American	3 (3.8)
White	72 (92.3)
Other	1 (1.3)
<b>Ethnicity, n (%)</b>	
Hispanic	3 (3.8)
Non-Hispanic	75 (96.2)
<b>Height (cm)</b>	
Mean (SD)	167.59 (10.2)
<b>Weight (kg)</b>	
Mean (SD)	64.73 (13.5)
<b>BMI (kg/m<sup>2</sup>)</b>	
Mean (SD)	22.95 (3.8)

Table 2. Overview of Parenteral Nutrition History

Characteristics	Enrolled Set (N = 78)
<b>Total Infusion Volume (mL) of PN/day or night</b>	
Mean (SD)	2614.9 (1151.77)
<b>Infusion Duration (minutes/days)</b>	
Mean (SD)	708.5 (124.13) or ~12 hours
<b>Number of Weeks from Start of PN to Screening – All Patients</b>	
Mean (SD)	482.3 (484.27) or ~9 years
<b>PN Frequency (days per week)</b>	
Mean (SD)	6.6 (0.95)
<b>Amino Acids (grams per day per week)</b>	
Mean (SD)	60.74 (33.47)
<b>Amino Acids (grams per kg day per week)</b>	
Mean (SD)	0.98 (0.54)
<b>Dextrose (kcal per day per week)</b>	
Mean (SD)	997.50 (595.31)
<b>Dextrose (kcal per kg day per week)</b>	
Mean (SD)	16.38 (11.42)
<b>Lipid Frequency (days per week)</b>	
Mean (SD)	3.0 (2.42)
<b>Lipid Types, n (%)</b>	
No Lipids	8/78 (10.3%)
Fish Oil Based	1/78 (1.3%)
Plant Based	38/78 (48.7%)
Mixed Oil	31/78 (39.7%)
<b>Lipids (grams per day per week)</b>	
Mean (SD)	18.72 (18.16)
<b>Lipids (grams per kg day per week)</b>	
Mean (SD)	0.31 (0.32)
<b>Vitamin B12 added each night, n (%)</b>	
Yes	78/78 (100.0)
<b>Folic Acid added each night, n (%)</b>	
Yes	78/78 (100.0)

Table 3. Overview of Choline Deficiency and Liver Injury

Characteristics	Enrolled Set (N = 78)
<b>Number of Patients with Choline Deficiency</b>	78.2% (61/78)
<b>Number of Patients with Liver Injury</b>	
All Patients	60.5% (46/76)
Choline Deficient Patients	63.3% (38/60)

Note: Choline Deficiency was defined as plasma free choline concentration  $< 9.5$  nmol/mL.  
Note: Liver injury was defined as elevated liver tests [ $> 1.5 \times$  ULN; ALP, AST, ALT, GGT, direct bilirubin, total bilirubin] or steatosis [MRI-PDFF  $\geq 8\%$ ].  
Note: Percentages are based on number of patients in the Enrolled Set with observed data.

## References

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