Parenteral Nutrition Outcomes of Patients with Short Bowel Syndrome after Discontinuing Teduglutide

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- Bernard Messing, MD

- Investigator-initiated project funded by NPS Pharmaceuticals
Background

- Severe short bowel syndrome (SBS) may result in parenteral nutrition (PN) dependence to avoid malnutrition and dehydration.
- PN dependence is associated with undesirable long-term complications.
- Strategies to reduce PN dependence in these patients are sorely needed.
- Teduglutide, an injectable analog of glucagon-like peptide 2, a gut hormone, was tested.
Teduglutide in Adult Patients with SBS 24 week treatment

**≥ 20% PN Volume Reduction**

- Placebo: 6%
- 0.05 mg/kg: 46% *
- 0.1 mg/kg: 25%

**≥ 20% PN Volume Reduction**

- Placebo: 30%
- 0.05 mg/kg: 63% *

Jeppesen, Gut, 2011 (84 subjects)

NPS Press release, MAY/2011, (86 subjects)
Purpose

Describe clinical outcomes for 12 months after stopping teduglutide

- In subjects who received the drug $\geq 28$ weeks
- In subset of drug responders, defined as $\geq 20\%$ reduction in PN volume from pre-drug to end of drug therapy

Hypothesis:
- Most subjects would require increase in PN volume back to baseline levels
Methods

• Regulatory approval from University of Pennsylvania
• Regulatory approval at participating sites
• 11/20 eligible sites participated
• Data reported on 39/53 eligible subjects, follow-up data on 37
• Deidentified data entered into secure, password-protected web site
Methods

• Data points
  – Small bowel & colon length, colon in continuity
  – Existing data from clinical visits at 0, 3, 6, 12 months after stopping drug
    • PN volume
    • Body mass index
  – Complications
    • Hospital admissions
    • Bloodstream infections
    • Emergency department visits
Sample

• Groups defined groups by change in PN volume (L/wk) by 12 m off-drug
  – INC= ↑PN volume
  – NEUT/DEC = no change or ↓PN volume

• Entire sample
  – 15 INC, 22 NEUT/DEC

• Drug Responders – obtained ≥20% ↓PN volume
  – 12 INC, 13 NEUT/DEC
Statistical Methods

- Descriptive statistics as median (range)[IQR]
- Nonparametric tests to compare medians, NEG vs. NEUT/DEC
- GEE to compare change in PN vol, change in BMI over time
- Poisson correlation to compare differences in complications
- Stepwise linear regression of variables predicting change in BMI
- SPSS-17.0 (SPSS, Chicago, IL)
- P<0.05 significant
Intestinal Anatomy
Entire Sample

- INC=15 vs. NEUT/DEC=22
  - 3 subjects came off PN on-drug & remained off PN
- No difference
  - Age
  - Gender
  - Time since GI surgery
  - Pre-drug citrulline
  - Drug dose
  - Drug duration
  - Change in citrulline on-drug
PN Volume over Time
Entire Sample

PN vol ↑ in INC subjects after stopping teduglutide, p<0.001; PN vol did not change in NEUT/DEC subjects
BMI Change After Stopping Teduglutide

Entire Sample

Median, IQR error bars.
BMI ↓ in INC, p<0.001; no change in NEUT/DEC subjects
# Complications

## Entire Sample

<table>
<thead>
<tr>
<th>Complications:</th>
<th>INC</th>
<th>NEUT/DEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bloodstream infections</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>• Emergency Dept visits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hospital Admissions</td>
<td>3/15</td>
<td>7/22</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>25</td>
<td></td>
</tr>
<tr>
<td><strong>median 0 [IQR 0-1.0]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What variables predict change in BMI at 12 months off drug?

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Bowel Length (cm)</td>
<td>0.01</td>
<td>0.003</td>
</tr>
<tr>
<td>Colon Length (cm)</td>
<td>0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline BMI (kg/m2)</td>
<td>-0.155</td>
<td>0.001</td>
</tr>
<tr>
<td>Change in PN Volume on Drug (L/week)</td>
<td>0.15</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Adjusted R2 = 0.587

Adjusted R2 = 0.669
DRUG RESPONDERS
Drug Responders

- INC (n=12) vs. NEUT/DEC (n=13)
- Age
  INC=45 vs. NEUT/DEC=55 years, p=0.04
- No difference
  - Gender
  - Time since GI surgery
  - Pre-drug citrulline
  - Drug dose
  - Drug duration
  - On-drug change citrulline
PN volume ↑ in INC subjects after stopping teduglutide, p<0.001; No change in NEUT/DEC subjects
Drug Responders
BMI Change After Stopping Teduglutide

Median, IQR error bars.
BMI ↓ in INC, p<0.001; no change in NEUT/DEC subjects
## Complications

### Drug Responders

<table>
<thead>
<tr>
<th></th>
<th>INC</th>
<th>NEUT/DEC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complications:</strong></td>
<td>13 complications in 3/12 subjects</td>
<td>5 complications in 3/13 subjects</td>
</tr>
<tr>
<td>Bloodstream infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency Dept visits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital Admissions</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Incidence rates/person year</strong></td>
<td>1.5*</td>
<td>0.38*, p&lt;0.01</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>18, median 0 [IQR 0-0.25]</td>
<td></td>
</tr>
</tbody>
</table>
What variables predict change in BMI at 12 months off drug?

<table>
<thead>
<tr>
<th></th>
<th>Beta</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon Length (cm)</td>
<td>0.008</td>
<td>0.002</td>
</tr>
<tr>
<td>Baseline BMI (kg/m2)</td>
<td>-0.200</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Adjusted $R^2 = 0.669$
Limitations

- Descriptive study
- Small sample size
- Some eligible sites did not participate
- Short observation time (12 months)
- Existing clinical data collected (no new measures)
- No body composition measures
Summary

- 15/37 subjects rapidly ↑ PN volume
- 22/37 subjects (13/25 drug responders) maintained stable BMI and on-drug PN volume reduction by 12 months off-drug
- Both anatomic factors (small bowel, colon length) and drug response (PN volume decrease) predicted change in BMI off-drug
Conclusions

• Some subjects who ↓ PN using teduglutide might be considered for a trial of drug withdrawal under close supervision of nutrition, hydration.

• Other subjects with shorter colon & large ↓ in PN volume on-drug may need to continue teduglutide indefinitely if they wish to sustain reduced PN volume.
Thank you