Nonalcoholic Fatty Liver Disease in the U.S.: Clinical Characteristics of Patients Enrolled in TARGET-NASH

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INTRODUCTION

- NAFLD is a global epidemic with 22% of adults and 10% of children having a diagnosis of non-alcoholic fatty liver disease (NAFLD)
- NAFLD is the most common cause of liver disease in North America
- NAFLD is associated with increased risk of type II diabetes and cardiovascular events
- NAFLD is a common cause of liver failure

METHODS

- TARGET-NASH is an observational study, initiated in 2016, of pediatric and adult patients with NAFLD managed at academic and community hospitals
- The medical record of consented patients including demographics, laboratory results, pathology, imaging data and patient-reported outcomes, is abstracted into a centralized data core
- Detailed demographics, patient comorbidities, medications and disease progression are assessed as adverse outcomes, including cardiovascular and neoplastic complications

RESULTS

<table>
<thead>
<tr>
<th>Characteristics of the adult cohort at enrollment</th>
<th>All Subjects (N=1301)</th>
<th>NAFL (N=316)</th>
<th>NASH (N=504)</th>
<th>NAFLD Cirrhosis (N=481)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>39.1</td>
<td>38.0</td>
<td>39.4</td>
<td>40.1</td>
</tr>
<tr>
<td>&lt;18-39 years</td>
<td>n=59</td>
<td>n=58</td>
<td>n=56</td>
<td>n=62</td>
</tr>
<tr>
<td>40-64 years</td>
<td>10.2%</td>
<td>11.1%</td>
<td>16.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>34.3%</td>
<td>35.6%</td>
<td>25.2%</td>
<td>42.9%</td>
</tr>
<tr>
<td>Sex, female</td>
<td>57.8%</td>
<td>51.6%</td>
<td>60.9%</td>
<td>58.5%</td>
</tr>
<tr>
<td>Median BMI (kg/m²)</td>
<td>32.0</td>
<td>29.0</td>
<td>32.0</td>
<td>33.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>43.7%</td>
<td>21.5%</td>
<td>37.3%</td>
<td>64.9%</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>19.8%</td>
<td>14.2%</td>
<td>17.1%</td>
<td>26.4%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>57.6%</td>
<td>49.7%</td>
<td>52.6%</td>
<td>68.0%</td>
</tr>
<tr>
<td>Anxiety or Depression</td>
<td>29.4%</td>
<td>19.0%</td>
<td>29.6%</td>
<td>36.0%</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>20.9%</td>
<td>15.2%</td>
<td>17.5%</td>
<td>28.3%</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea Syndrome</td>
<td>19.3%</td>
<td>6.7%</td>
<td>19.0%</td>
<td>27.7%</td>
</tr>
<tr>
<td>Medication: pioglitazone</td>
<td>3.5%</td>
<td>2.8%</td>
<td>3.4%</td>
<td>4.0% 0.4114</td>
</tr>
<tr>
<td>Medication: metformin</td>
<td>31.5%</td>
<td>17.8%</td>
<td>28.7%</td>
<td>42.8%</td>
</tr>
<tr>
<td>Supplement: vitamin E</td>
<td>14.1%</td>
<td>8.2%</td>
<td>15.6%</td>
<td>16.1%</td>
</tr>
</tbody>
</table>

MEDICATED INTERVENTIONS

- Nonalcoholic fatty liver disease (NAFLD) is highly prevalent in both children and adults
- NAFLD can lead to cirrhosis, hepatocellular carcinoma and death from liver disease
- NAFLD is associated with increased risk of type II diabetes and cardiovascular events
- Current treatment goals, limited to exercise and weight loss, are difficult for many patients to achieve and maintain. Thus, pharmacological therapies are greatly needed; many are in various stages of development.
- Large, observational cohorts are needed to better understand the spectrum of NAFLD by obtaining real-world data that avoids ascertainment bias from studies in tertiary care centers alone and allows for further validation of histology and non-invasive biomarkers.
- The overall aim of TARGET-NASH is to determine the natural history of NAFLD and to evaluate treatment regimens used in real world clinical practice.
- This current analysis describes the baseline characteristics of consecutive patients enrolled to date in TARGET-NASH.

TARGET-NASH SITES

DISEASE CATEGORY DEFINITIONS

NAFL
- Any participant not meeting criteria for clinical NASH or cirrhosis

NASH
- Confirmed by biopsy:
  - Steatohepatitis by Brunt OR
  - NAS total score ≥ 4
- Clinical diagnosis:
  - Adults: ALT > 19 U/L for female, > 30 U/L for men and;
  - Hepatic steatosis on biopsy or CT/MRI and;
  - ≥ 1 of the following: BMI ≥ 30, type II diabetes, dyslipidemia

NAFLD
- 1) Liver biopsy with fibrosis stage = 4 OR
- Cirrhosis
  - 2) Liver biopsy with fibrosis stage = 3 and 1 ≥ clinical signs of cirrhosis OR
  - 3) 2 or more clinical signs of cirrhosis OR
  - 4) FibroScan® stiffness result ≥ 11 kPa

SUMMARY

- In the adult cohort, 76% of the first 1301 consecutive patients enrolled had NASH/NAFLD cirrhosis.
- Similarly, 85% of the first 152 pediatric patients enrolled had NASH/NAFLD cirrhosis.
- Metabolic syndrome risk factors like diabetes, hypertension and obesity are present in greater proportions in NASH and NAFLD cirrhosis.
- Comorbid conditions that make lifestyle intervention difficult (namely, anxiety / depression, osteoarthritis and cardiovascular disease) occur at significantly greater rates as disease severity increases.

CONCLUSIONS

- Participants enrolled in TARGET-NASH include populations, such as patients with cirrhosis and cardiovascular disease, not widely represented in clinical trials.
- Real-world clinical registries are important for obtaining unbiased natural history data and determining clinical effectiveness of new interventions.
- TARGET-NASH will be an important source of real world patient oriented outcome data.

STATEMENT AND DISCLOSURES

TARGET-NASH is a collaboration among academic & community investigators, the pharmaceutical industry, and NASH patient community advocates. TARGET-NASH is sponsored by TARGET Pharmaceuticals, Inc. TARGET thanks the study staff, nurses, health care providers and patients at each study center for their contributions to this work.

Listings of Principal Investigators and Industry Partners are available upon request by emailing info@targetpharmaceuticals.com.