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

TARGET PharmaSolutions

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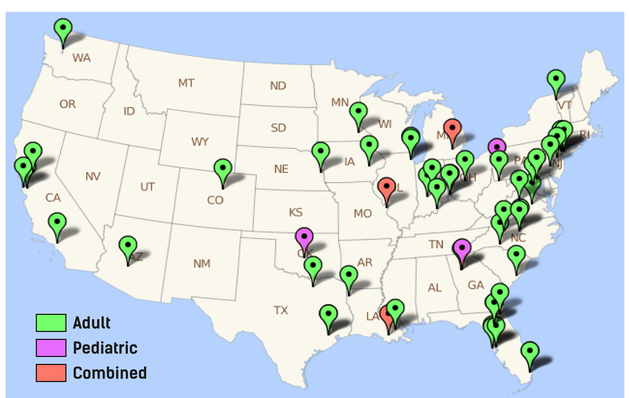
INTRODUCTION

- 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 also 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.

METHODS

- TARGET–NASH is an observational study, initiated in 2016, of pediatric and adult patients with NAFLD managed at academic and community Hepatology, GI and Endocrinology practices.
- The medical record from consented patients including narratives, 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 are adverse outcomes, including cardiovascular and neoplastic complications.
- Data from the first 1301 consecutively enrolled patients are presented. Descriptive statistics with ANOVA and Cochran–Armitage tests for trend are reported.

TARGET–NASH SITES



RESULTS

Characteristics of the adult cohort at enrollment

	All Subjects (N=1552)	NAFL (N=377)	NASH (N=594)	NAFLD Cirrhosis (N=581)	P-value[2]
Median Age (years)[1]	**n=59**	**n=59**	**n=56**	**n=62**	
18–39 years 40–64 years >=65 years	**9.6%** **55.8%** **34.6%**	**10.9%** **54.1%** **35.0%**	**14.8%** **59.6%** **25.6%**	**3.4%** **53.0%** **43.5%**	**<0.0001**[a]
Sex, Female	**57.8%**	**53.3%**	**60.3%**	**58.2%**	**0.0998**[b]
Median BMI (kg/m^2)	**32.0**	**29.0**	**32.0**	**33.0**	**<0.0001**[a]
Diabetes	**43.9%**	**21.2%**	**37.4%**	**65.4%**	**<0.0001**[c]
Cardiovascular Disease	**20.0%**	**13.8%**	**17.0%**	**27.0%**	**<0.0001**[c]
Hypertension	**57.7%**	**49.3%**	**52.9%**	**68.2%**	**<0.0001**[c]
Anxiety or Depression	**28.8%**	**18.8%**	**29.1%**	**34.9%**	**<0.0001**[c]
Osteoarthritis	**20.7%**	**15.4%**	**17.2%**	**27.7%**	**<0.0001**[c]
Obstructive Sleep Apnea Syndrome	**19.8%**	**7.2%**	**19.2%**	**28.7%**	**<0.0001**[c]
Medication: Pioglitazone	**3.6%**	**2.7%**	**3.7%**	**4.1%**	**0.2434**[c]
Medication: Metformin	**31.1%**	**17.5%**	**28.5%**	**42.7%**	**<0.0001**[c]
Supplement: Vitamin E	**13.7%**	**6.6%**	**15.2%**	**16.7%**	**0.0001**[c]

[1] Age calculated based on year of consent minus birth year

[2] Tests of homogeneity or trend:
[a] ANOVA test
[b] Likelihood Ratio test
[c] Cochran–Armitage test

Characteristics of the pediatric cohort at enrollment

- Number enrolled = **193**
- Median age = **14**
- Sex, female = **28.5%**
- Median BMI = **32.0**
- NAFL = **18.1%**
- NASH = **77.7% (24% biopsy confirmed)**
- NAFLD Cirrhosis = **4.1%**

DISEASE CATEGORY DEFINITIONS

NAFL	Any participant not meeting criteria for clinical NASH or cirrhosis
NASH	Confirmed by biopsy: • Steatohepatitis by Brunt criteria OR NAS total score ≥ 4 Clinical diagnosis: • ALT > 19 U/L for adult female (22 child), > 30 U/L for adult male (26 child) and; • Hepatic steatosis on biopsy or CT/US/MRI and; • ≥ 1 of the following: BMI ≥ 30, type II diabetes, dyslipidemia
NAFLD Cirrhosis	1) Liver biopsy with fibrosis stage = 4 OR 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 1552 consecutive patients enrolled had NASH/NAFLD cirrhosis.
- Similarly, 82% of the first 193 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 & DISCLOSURES

TARGET–NASH is a collaboration among academic & community investigators, the pharmaceutical industry, and NASH patient community advocates. TARGET–NASH is sponsored by TARGET PharmaSolutions, 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@targetpharmasolutions.com.