Real World Evidence Showing High Rates of Cardiovascular Events in NAFLD Patients Regardless of Liver Disease

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EASL The Home of Hepatology | THE INTERNATIONAL LIVER CONGRESS™ 2018 APRIL 11-15, PARIS, FRANCE

INTRODUCTION

- Nonalcoholic fatty liver disease (NAFLD) affects approximately 30% of the adult population in North America.
- NAFLD is associated with increased cardiovascular (CV) events and mortality.
- Most of the existing data are derived from tertiary care centers.
- There is a need for data to confirm the prevalence of CV disease in those with NAFLD managed in usual clinical practice.

AIM

To define the profile of CV risk factors in those with nonalcoholic fatty liver (NAFL), nonalcoholic steatohepatitis (NASH), and NAFLD cirrhosis in a real-world cohort of participants with NAFLD.

METHODS

- TARGET-NASH is a prospective study of participants with the entire spectrum of NAFLD and is inclusive of patients typically excluded from clinical trials due to comorbidities, disease stage, etc.
- Participants are enrolled at academic and community sites.
- Participants were categorized using commonly implemented, pragmatic case definitions. See Phenotype Disease Definitions.
- CV events were defined as acute progressions of CV disease or cardiac or vascular intervention.
- CV disease history was defined as any cardiac or vascular condition excluding hypertension and congenital conditions
- A multivariable regression analysis was performed to identify factors associated with CV events.

Disease Phenotype Definitions

NAFL	**Any participant with evidence of fatty liver but not meeting criteria for clinical NASH or NAFLD cirrhosis**
NASH	**Confirmed by biopsy:** • **Steatohepatitis by Brunt criteria OR NAS total score ≥ 4** **Clinical diagnosis:** • **ALT > 19 U/L female, > 30 U/L male and;** • **Hepatic steatosis on biopsy or CT/US/MRI and;** • **≥ 1 of the following: BMI ≥ 30, type 2 diabetes, dyslipidemia**
NAFLD Cirrhosis	**History of NAFLD with:** **Liver biopsy with fibrosis stage = 4 OR** **Liver biopsy with fibrosis stage = 3 and 1 ≥ clinical signs of cirrhosis OR** **2 or more clinical signs of cirrhosis OR** **FibroScan® stiffness result ≥ 11 kPa**

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.

Arun Sanyal, MD disclosures: grants from Conatus, Gilead, Malinckrodt, Salix, Novartis, Galectin, BMS, Merck, and Sequana; advisor for Sanyal Bio Conatus, Gilead, Malinckrodt, Pfizer, Salix, Boehringer Ingelheim, Nimbus, Nitto Denko, Hemoshear, Lilly, and Ardelyx

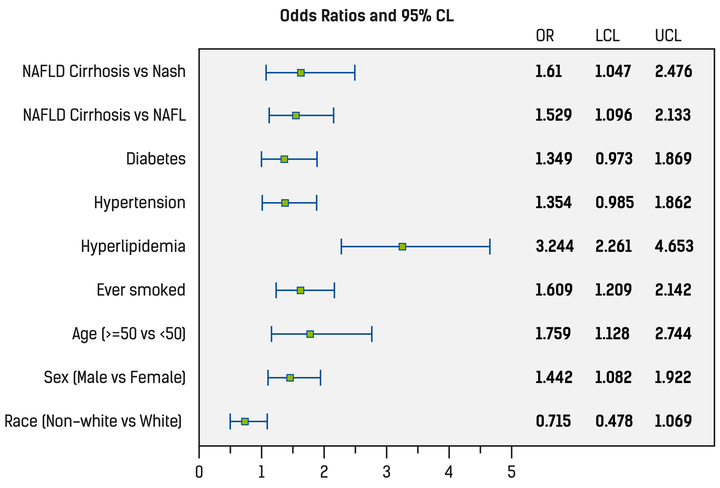
Anna S. Lok, MD disclosures: grants from BMS, Gilead, and TARGET PharmaSolutions; advisor for Reseverlogix, Spring Bank, and Viravaxx

RESULTS

Characteristics at Enrollment

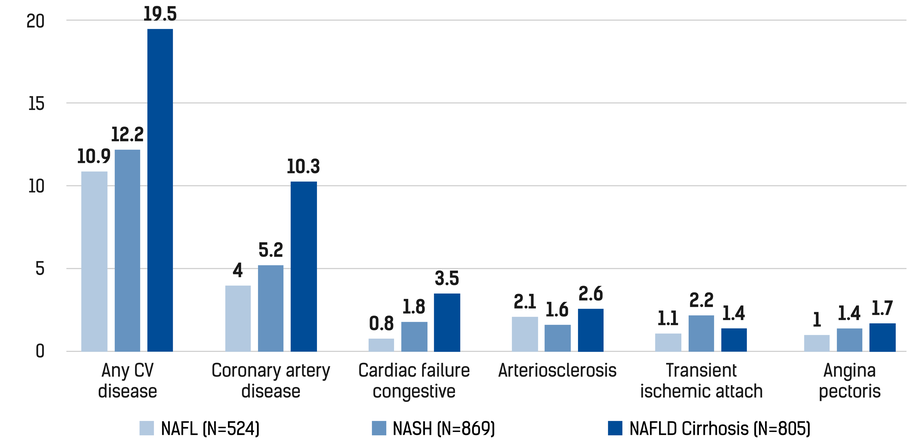
	NAFL (N=524)	NASH (N=869)	NAFLD Cirrhosis (N=805)
Median Age Min-Max <50 years % ≥50 years %	59.0 18.0 – 87.0 27.6 72.4	56.0 18.0 – 91.0 33.3 66.7	63.0 19.0 – 87.0 14.1 85.9
Sex, Female %	53.3	61.4	58.8
Race, White %	55.5	68.2	87.5
% BMI ≥ 32	36.4	55.6	59.2
Type II Diabetes %	27.3	43.2	68.4
Hypertension %	42.4	51.8	63.0
Hyperlipidemia %	40.1	57.1	57.4
Sleep Apnea %	8.0	19.7	28.2
Ever Smoked %	43.7	49.9	52.2
CV Disease History %	10.1	12.3	19.8
CV Event %	7.1	9.3	16.4

Risk Indicators for Any CV Event

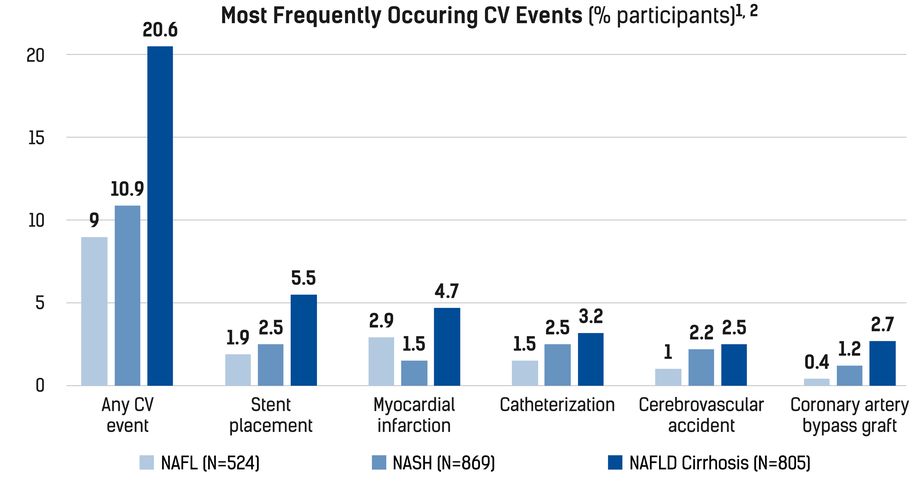


Note: ORs and CLs are from a forward, step-wise logistic regression model (significance level for entry=.25, significance level to remain in the model=0.1) fit with the following predictors of any CV event: disease phenotype, diabetes, hypertension, hyperlipidemia, ever smoked, daily vitamin E use >= 800 IU, sleep apnoea, AUDIT score > 7, age at study entry (dichotomous response), BMI at enrollment (dichotomous response), gender and race (dichotomous response). The final model includes the following risk indicators for any CV event: hyperlipidemia, disease severity, ever smoked, age at study entry, sex, hypertension, diabetes, race.

Most Frequently Occuring CV Disease History (% participants)[1]



Most Frequently Occuring CV Events (% participants)[1, 2]



1 Participants are counted once in each term for which they have documented history
2 CV Events of coronary artery bypass, stent placement and catheterization are assumed to be non-exclusive and of decreasing severity. Thus, participants are counted only once – in the category of greatest severity – for these three events. For example, a participant who has coronary artery bypass and stent placement is counted once for coronary artery bypass and is not counted for stent placement.

CONCLUSIONS

- In this real world cohort representing the full spectrum of NAFLD, there was a high proportion of participants who have experienced >1 CV events
- In a joint model with other population characteristics, NAFLD severity was associated with increased risk of CV events.
- These events reflect clinically meaningful outcomes including those related to coronary artery disease, congestive heart failure, and cerebrovascular accidents