Characterization of Polypharmacy in Patients with NAFLD

TARGET–NASH

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INTRODUCTION

- Polypharmacy in patients with NAFLD is common but the magnitude of this problem has not been described.
- It is still not clear if there are certain drugs that might accelerate or slow disease progress.
- As therapies for NAFL and NASH become available, the baseline use of multiple medications may increase the risk of drug–drug interactions (DDI). Therefore, knowing the prevalence of using drugs metabolized by specific pathways may be helpful in drug development and predicting DDI.

METHODS

- TARGET–NASH is a longitudinal observational study of participants followed at 55 sites (40 academic/15 community) in the U.S., and includes patients across the entire spectrum of NAFLD.
- Data from medical records (including narratives, labs, imaging, pathology, procedures, and outcomes) are centrally abstracted and monitored for completeness and accuracy.
- Of the 4,293 participants enrolled in TARGET–NASH, 3,671 are included in this data analysis and includes each phenotype category displayed on the results table. Medication use reviewed was within a +/– 30 window of the enrollment date.
- Participants were grouped by disease severity (NAFL, NASH, NAFLD cirrhosis) as defined by pragmatic case definitions.

DISEASE CATEGORY DEFINITIONS

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	History of NAFLD with: 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® elastography result ≥ 11 kPa
NAFL	Any participant not meeting criteria for clinical NASH or cirrhosis

STATEMENT & DISCLOSERS

RESULTS

Demographics and Baseline Characteristics in TARGET–NASH Participants

SUMMARY	NAFLD Cirrhosis		NASH		NAFL		All Participants
	Adult (N = 1279)	Pediatric (N = 12)	Adult (N = 1317)	Pediatric (N = 279)	Adult (N = 688)	Pediatric (N = 96)	N = 3671
Median Age (years)	62.0	13.5	55.0	14.0	58.0	13.5	57.0
Gender (%) Female Male	58.9 41.1	33.3 66.7	62.2 37.8	32.3 67.7	52.9 47.1	26.0 74.0	56.0 44.0
Race, % White Black Asian	87.6 2.7 3.7	100.0 0.0 0.0	71.9 6.8 12.5	65.2 3.2 1.8	54.4 7.3 0.3	80.2 4.2 1.0	73.9 5.1 11.2
BMI, % >30–35	27.7	33.3	29.4	29.9	17.6	30.2	26.7

Adult and Pediatric TARGET–NASH Participants: Medications Used Per Participant

NAFL
N=784 Participants
Median = 5 Meds Used

NASH
N=1596 Participants
Median = 7 Meds Used

Cirrhosis
N=1291 Participants
Median = 11 Meds Used

Medication Used

Most Frequently Used Medications in TARGET–NASH Participants

| | NASH/NAFL | Cirrhosis |

	PPI	Vitamin D	Statin	ACEI	ARB Renin	H1RA	Insulin	NSAID
ADULT	35.9	32.4	34.9	17.7	18.3	15.0	8.4	12.4
	52.0	41.4	37.6	25.1	19.7	19.5	31.4	16.0
PEDS	8.0	19.7	1.3	2.4	0.8	16.8	1.1	10.1
	52.0	41.7		8.3		25.0	8.3	25.0

Most Frequently Used Medications in TARGET–NASH Participants (continued)

| | NASH/NAFL | Cirrhosis |

	Opiate	SSRI	Diuretic Aldo	Benzo-diazepine	Vitamin E	Fibrate	Antioxidant
ADULT	12.4	12.3	4.6	13.3	9.8	13.0	9.9
	18.4	17.0	28.7	14.1	13.4	10.3	14.7
PEDS	1.6	5.6		1.6	8.5	1.9	0.8
		16.7			33.3		

* = p-value <0.05. ** = p-value < 0.001. P-values are from a chi-square test of the association between disease category (NASH/NAFL vs Cirrhosis) and medication use.

SUMMARY & CONCLUSIONS

- Polypharmacy is common in patients with NAFLD/NASH and the number of medications used increases with disease severity.
- The relationship between medications and the underlying disease state are unclear. It is likely that the use of certain medications is necessitated by the underlying conditions that led to NAFL/NASH/cirrhosis, rather than contributing or causing advanced fibrosis.
- It should be noted that certain medications, such as diuretics (aldosterone antagonist) and non–selective beta blockers, are used with increased frequency in cirrhosis due to the concomitant complications.
- Further analysis of this dataset may allow prediction of drug–drug interactions with future agents developed to treat NASH and facilitate targeting therapies based on mechanistic considerations.