



## Introduction

- Liver biopsy is the gold standard for assessing the histologic features of NASH.
- The utility of a biopsy is dependent on the accuracy of its interpretation and whether all essential features are reported.
- Useful reporting should clearly document steatosis, inflammation, hepatocyte ballooning and fibrosis or the lack thereof.
- The aim of this study is to describe completeness of real-world NASH-related pathology reports and the concordance of findings with a central expert pathologist.

## Methods

- TARGET-NASH is a longitudinal real-world cohort of patients with NAFLD.
- Liver histology reports from academic and community practices were analyzed for documentation of steatosis, lobular inflammation, portal inflammation, hepatocyte ballooning and fibrosis stage.
- The presence of a standardized scoring system (NAFLD activity score [NAS] or Brunt Score) and the local pathologist's overall interpretation were recorded.
- A subset of biopsy slides was overread by a central expert pathologist.
- Descriptive analysis and pathologists' concordance for quantifying steatosis, inflammation, ballooning and fibrosis, assessed using weighted kappa statistics, are reported.

**Table 1. Baseline Characteristics – NASH Patients**

Summary	All Patients (N = 221)	Academic (N = 167)	Community (N = 54)
<b>Age at Study Entry (years)</b>			
Median (n)	53.0 (153)	51.0 (113)	56.5 (40)
Min – Max	10.0 - 75.0	10.0 - 75.0	24.0 - 71.0
<b>Gender, n (%)</b>			
n	153	113	40
Female	87 (56.9%)	65 (57.5%)	22 (55.0%)
<b>Race, n (%)</b>			
n	144	104	40
White	122 (84.7%)	89 (85.6%)	33 (82.5%)
Black or African American	8 (5.6%)	2 (1.9%)	6 (15.0%)
Asian	6 (4.2%)	5 (4.8%)	1 (2.5%)
Other	8 (5.6%)	8 (7.7%)	0 (0.0%)
Not Available	9	9	0
<b>Ethnicity, n (%)</b>			
n	152	112	40
Hispanic or Latino	35 (23.0%)	30 (26.8%)	5 (12.5%)
Not Hispanic or Latino	116 (76.3%)	81 (72.3%)	35 (87.5%)
Other	1 (0.7%)	1 (0.9%)	-
Not Available	1	1	0
<b>Site Type, n (%)</b>			
n	153	113	40
Academic	113 (73.9%)	113 (100.0%)	-
Community	40 (26.1%)	-	40 (100.0%)

## Conclusions

- **There is substantial heterogeneity in the histological reporting of NASH in the real world with a large proportion of reports missing important descriptors of NASH disease activity.**
- **There is discordance between interpretation by site pathologists (academic and community) and a central pathologist.**
- **At best there is only moderate concordance for fibrosis staging.**
- **Such heterogeneity and lack of reliability in histologic reporting and interpretation may adversely impact patient assessment and application of new NASH therapies.**

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## Results

- A total of 153 pathology reports from 14 sites with a diagnosis of NASH were reviewed.
- Documentation on steatosis, lobular inflammation, portal inflammation and ballooning were missing from 39%, 46%, 52% and 46% of reports, respectively.
- Grading of NASH components was more commonly performed using the NAS compared to the Brunt criteria (65% vs 24%), but a standardized grading system was missing in 21% of reports.
- 75 digitized biopsy slides were interpreted by a central pathologist and compared to reports from local pathologists at TARGET-NASH sites.
- There was significant discrepancy in grading of NASH components and fibrosis staging (Table 2).
- Weighted kappa scores showed poor to fair concordance for steatosis, lobular inflammation, portal inflammation, and hepatocyte ballooning.
- Concordance for NAS and Brunt grading was fair.
- There was moderate agreement for fibrosis staging.

**Table 2. Kappa Statistics for Concordance of Histological Interpretation in NASH for Central vs Local Read of Biopsies**

Histological Characteristic	Number of Pathology Reports Compared	Weighted Kappa Statistic (95% CI)	Concordance Interpretation
Steatosis	57	0.364 (0.2029, 0.5242)	Fair
Lobular Inflammation	29	-0.081 (-0.1847, 0.0220)	Poor
Portal Inflammation	31	0.210 (-0.0376, 0.4580)	Fair
Hepatocyte Ballooning	26	0.117 (-0.0708, 0.3038)	Slight
Fibrosis Stage	69	0.575 (0.4603, 0.6894)	Moderate
<b>Scoring System</b>			
NAFLD Activity Score	38	0.237 (0.0591, 0.4150)	Fair
Brunt Grade (Inflammation)	26	0.384 (0.1591, 0.6082)	Fair
Brunt Stage (Fibrosis)	69	0.590 (0.4775, 0.7019)	Moderate