Vanderbilt Transplant Nurse Practitioner Symposium
Nonalcoholic Fatty Liver Disease (NAFLD) – How Fatty Liver Can Impact the Liver Transplant Recipient

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Prevalence of Self-Reported Obesity Among Adults 2015

% of adults with BMI ≥ 30 Kg/m²
Facts about NAFLD

• NAFLD affects about 17% - 46% of adults in Western countries (parallels the metabolic syndrome – MetS)
• NAFLD affects ~7% of individuals with lean body mass
• NASH may be present in 2%-3% of the US population
• About 60% of patients >50 yrs of age with diabetes or obesity probably have NASH with advanced stage fibrosis.
• Identification of NASH is by liver biopsy, but biomarkers to detect advanced fibrosis are becoming increasingly reliable.
• In patients with NASH – half of the deaths are due to CV disease and malignancy; third leading cause of death is cirrhosis.
• The incidence of NAFLD-related HCC is increasing and >50% of cases occur in the absence of cirrhosis.
## Prevalence of NASH Versus HCV

<table>
<thead>
<tr>
<th></th>
<th>Percent of Total US Population</th>
<th>Number of Persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>US population</td>
<td>–</td>
<td>322 million¹</td>
</tr>
<tr>
<td>NAFLD</td>
<td>10%–35%²</td>
<td>32–113 million</td>
</tr>
<tr>
<td>NASH</td>
<td>3%–5%²</td>
<td>10–16 million</td>
</tr>
<tr>
<td>Chronic HCV</td>
<td>1%³</td>
<td>3.2 million</td>
</tr>
</tbody>
</table>
NAFLD Underrecognized in the Primary Care Setting

Proportion of Patients Receiving Components of NAFLD Care

- 39.4% Documented as having abnormal transaminases
- 21.5% Given NAFLD as possible diagnosis
- 14.7% Counseled on diet and exercise
- 10.4% Referred to a specialist

Only the magnitude and proportion of ALT elevation were predictive of receiving NAFLD care.

Blais et al. Am J Gastroenterol 2015
Facts about NAFLD

• Lifestyle modification is the foundation of treatment for patients with NAFLD
• Available treatments of proven benefit for NASH including vitamin E, pioglitazone, obeticholic acid, but effect size is modest (< 50%) and none are approved by the FDA.
Nonalcoholic Fatty Liver Disease

- Simple steatosis
- Steatohepatitis
- Exclusion of alcohol intake (< 20 grams per day)
Nonalcoholic Steatosis

Definition

• Macrovesicular fatty change without lobular or portal inflammation, hepatocyte injury, or fibrosis

• Absence of other causes of liver disease
Nonalcoholic Steatohepatitis (NASH)  

**Definition**

- Histological picture that resembles alcohol-induced liver injury
- Defined by steatosis and necroinflammation with or without Mallory bodies or fibrosis
- Exclusion of other diseases associated with steatosis
Conditions Associated with Fatty Liver

- Metabolic syndrome (obesity, diabetes, hypertension, hypertriglyceridemia)
- Metals – barium salts, borates, chromates, phosphorus, thallium & uranium compounds
- Cytotoxic drugs – L-asparaginase, methotrexate
- Other drugs – HAART, bleomycin, tetracycline, amiodarone, estrogens, glucocorticoids, coumadin, tamoxifen, methotrexate
- Metabolic disorders – IBD, small bowel (JI) bypass, starvation, Kwashiorkor, TPN
- Infections – HIV, HCV (genotype 3)
Conditions Associated with Fatty Liver

Inborn Errors of Metabolism

- Abetalipoproteinemia
- Familial hepatosteatosis
- Galactosemia
- Glycogen storage disease
- Hereditary fructose intolerance
- Homocystinuria
- Systemic carnitine deficiency
- Tyrosinemia
- Weber-Christian syndrome
- Wilson disease
- Lysosomal acid lipase deficiency
Natural History of NAFLD

• The incidence of fibrosis in NAFLD
  – 30% - 40% will develop advanced fibrosis
  – up to 20% will develop cirrhosis

• Obesity, diabetes and increased age are independent predictors of fibrosis

• About 30% - 40% progress from steatohepatitis to fibrosis over 4 yrs

• Estimated 9% - 20% of NASH patients develop cirrhosis
NAFLD – Disease Progression

Excess fat builds up in the liver cells

Inflammatory form of the condition with liver cell injury

Time to Progression ~10 years

~25%

9%-20%

Liver Cirrhosis

Hepatocellular Cancer (~3% per year)

Liver Failure (40-60%)

Liver Transplant (~25%)

~ 5-10 years
Causes of Cirrhosis

- Viral Hepatitis B & C: 10%
- Hemochromatosis: 5%
- Biliary Disease: 5%
- Other: 5%
- Other: 5%
Trends in NASH-Related Liver Transplantation Waitlist Registrations

- In 2013, NASH became 2nd indication for LT listing
- OR for waitlist mortality at 90 days
  - NASH: 1, reference
  - ALD: 0.77; \( P < .001 \)
  - HCV: 0.99; \( P = .92 \)
- Compared with HCV, NASH patients had the lowest chance of getting transplanted in 90 days and 1 year

Annual Trends in Adult Liver Transplant in US

UNOS/OPTN Registry
## Predictors of Fibrosis in Patients with NASH

<table>
<thead>
<tr>
<th>Factors</th>
<th>Angulo</th>
<th>Harrison</th>
<th>Ratziu</th>
<th>Dixon</th>
<th>Angulo</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Age</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>AST or ALT</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>ALT</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>HbA1c</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Insulin resistance index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Albumin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
Risk Factors for NASH & More Progressive Liver Injury

- Obesity (central)
- Hypertension
- Dyslipidemia
- Type 2 diabetes mellitus
- Metabolic syndrome
Apple or Pear
Central Obesity
Risk of NASH Based on Presence of Metabolic Factors

- No DM or HTN: 8%
- HTN: 31%
- DM: 62%
- DM + HTN: 73%

Metabolic Syndrome

Identify metabolic syndrome and treat, if present, after 3 months of TLC.

Clinical Identification of the Metabolic Syndrome – Any 3 of the Following:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal obesity*</td>
<td>Waist circumference†</td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm (&gt;40 in)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 in)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≥150 mg/dL</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&lt;40 mg/dL</td>
</tr>
<tr>
<td>Women</td>
<td>&lt;50 mg/dL</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>≥130/≥85 mmHg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>≥110 mg/dL</td>
</tr>
</tbody>
</table>

*Abdominal obesity: Men with a waist circumference of >102 cm (>40 in) and Women with a waist circumference of >88 cm (>35 in).
†Waist circumference: ≥102 cm (>40 in) for Men and ≥88 cm (>35 in) for Women.

National Cholesterol Education Program  TLC – therapeutic lifestyle changes
Comorbidities That Increase CV Risk in NAFLD

- Oxidative stress
- Inflammation
- Cytokine abnormalities
- Hypertension
- Obesity
- T2 Diabetes mellitus
- Subclinical atherosclerosis
- Coronary /abdominal aortic calcification
- Obstructive sleep apnea
- Impaired LV function
- Heart failure
- Epicardial fat
- Peripheral artery disease
- Chronic kidney disease
- Hyperuricemia
- Rheumatoid arthritis
- SLE
- Psoriasis
- Erectile dysfunction

Katsiki et al. Metabolism 2016
Prevalence of Metabolic Syndrome

NHANES III

Oh et al. *Aliment Pharmacol Ther* 2008

Survival with NAFLD & MetS

Fig. 1 – The cumulative survival in different study groups as Kaplan–Meier trend. Abbreviations: NAFLD, non-alcoholic fatty liver disease; MetS, metabolic syndrome.

Karajamaki et al. Metabolism 2016
Liver Biopsy – Cirrhosis
Liver Biopsy - Conclusions

• Liver enzymes are a poor surrogate for determining the severity of NAFLD

• Liver biopsy is required to make the diagnosis of NASH

• Patients with NASH and fibrosis are at greatest risk for disease progression

• Current noninvasive tests are best suited for ruling advanced fibrosis in or out
  – Data are not supportive for differentiating simple hepatic steatosis from NASH with milder degrees of fibrosis
Risk of Developing Advanced Fibrosis

Inflammation on Initial Liver Biopsy

N= 221 patients

Caldwell & Argo  *Digestive Diseases* 2010
What Are the Clinical Predictors of Liver-Related Mortality in NAFLD?

- Database of histologic NAFLD (N = 289)
- Clinicodemographic data from the time of biopsy
  - NASH (59.2%)
  - NASH patients were predominantly female, had higher AST/ALT, and higher fasting serum glucose
- During median follow-up at 150 months, NASH patients had higher risk of liver-related mortality than non-NASH NAFLD

### What Are the Histologic Predictors of Liver-Related Mortality in NAFLD?

#### Univariate Survival Analyses

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portal inflammation (grade ≥2)</td>
<td>6.68 (2.20–20.3)</td>
<td>.0008</td>
</tr>
<tr>
<td>Ballooning (grade ≥2)</td>
<td>5.32 (1.89–14.9)</td>
<td>.0015</td>
</tr>
<tr>
<td>MD bodies (grade ≥2)</td>
<td>4.21 (1.66–10.7)</td>
<td>.0024</td>
</tr>
<tr>
<td>Portal fibrosis (grade &gt;2)</td>
<td>14.1 (5.47–36.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pericellular fibrosis (grade &gt;2)</td>
<td>4.86 (1.73–13.7)</td>
<td>.0027</td>
</tr>
</tbody>
</table>

On multivariate analysis, only significant fibrosis (grade ≥3) was an independent predictor of LRM.

Younossi et al. *Hepatology* 2011
Prognosis Based on Liver Histology

- Fibrosis
- Portal inflammation
- NASH
- Ballooning

- Higher prognostic value
- Lower prognostic value

Loomba & Chalasani *Gastroenterology* 2015
The PRELHIN Study—Multivariate Analysis for Liver-Related Events by Fibrosis Stage

- **Stage 4**: 47.46 (11.94–188.61; P < .001)
- **Stage 3**: 13.78 (4.35–43.65; P < .001)
- **Stage 2**: 7.51 (2.26–24.94; P = .001)
- **Stage 1**: 2.38 (0.63–8.91; P = .198)
- **Stage 0** (reference)

Hazard ratios with 95% CI.
NAFLD - Mortality

- Liver-related complications
- Cardiovascular risk factors
- Increased risk of hepatocellular carcinoma and intrahepatic cholangiocarcinoma*
- Increased risk of colorectal cancer*

*SEER-Medicare Database
* Wong et al. Gut 2011
NAFLD and Hepatocellular Cancer

NAFLD Is an Increasingly Important Cause of HCC with Higher Mortality

- Cases of HCC in the United States: data from surveillance, epidemiology and end results (SEER)-medicare registries (2004–2009)
- Cohort included 4979 cases of HCC and 14,937 non-HCC matched controls (3:1)

Proportion of Liver Diseases in HCC Portion of Cohort

- HCV: 54.9%
- ALD: 16.4%
- NAFLD: 14.1%
- HBV: 9.5%
- Other: 5.1%

Abbreviations: ALD, alcoholic liver disease; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, nonalcoholic fatty liver disease.

Obesity & Metabolic Syndrome

• These terms are not synonymous
• Which of the individual components have the greatest impact (e.g. insulin resistance/diabetes mellitus, dyslipidemia, hypertension, obesity)?
• Metabolic syndrome may be more important than the sum of its parts
# Pretransplant Prevalence of Metabolic Syndrome and Obesity

<table>
<thead>
<tr>
<th>Organ</th>
<th>Metabolic Syndrome (MS) or Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>10% obesity</td>
</tr>
<tr>
<td>Kidney/Pancreas</td>
<td>59% MS</td>
</tr>
<tr>
<td>Liver</td>
<td>12% - 21% obesity</td>
</tr>
<tr>
<td>Heart</td>
<td>17% - 28% MS</td>
</tr>
<tr>
<td>Lung</td>
<td>12% obesity</td>
</tr>
</tbody>
</table>
How Obesity and Hepatic Steatosis Affect Liver Tx

• Operative issues
• Early post-surgical risks
• Increased patient morbidity and mortality after surgery in unselected patients
• Recurrent steatohepatitis
• Increase risk of recurrent or de novo metabolic complications and CV risks
• Allograft dysfunction and survival associated with donor steatosis
Obesity & Liver Transplant Outcomes
Postoperative Complications in Obese Patients

- Incisional hernia
- Wound infection
- Hematoma
- Abscess
- Bile leak
- Hepatic artery thrombosis
- Portal vein thrombosis
- Respiratory failure

Nair et al. Am J Gastroenterol 2001
Cox-Mantel test – no statistical differences between groups

Nair et al. Am J Gastroenterol 2001
Morbidity & Mortality in Obese Patients After Liver Transplant

- Greater number of post-operative complications in severely obese patients (BMI > 31)
  - Respiratory failure ($p = 0.009$)
  - Systemic vascular complications ($p = 0.04$)
- Length of hospital stay after LTx higher for obese and severely obese patients
- Median cost:
  - Non-obese patients  $100,000$
  - Severely obese patients  $134,000$

Nair et al. Am J Gastroenterol 2001
Risk of Death After Liver Tx in Patients Based on BMI

* $P < 0.05$ in comparison to the reference group 19-22 kg/m²

Rustgi et al. Clinical Transplant 2004
Obesity and Liver Transplantation

• Perioperative morbidity
  – Prolonged operative time
  – Increased days in the ICU
  – Increased transfusion requirements
  – More infections and biliary complications
  – Decreased patient and graft survival (class II obese individual 35 – 40 kg/m²)

• Obese cirrhotic patients more likely to be turned down for organ offers

LaMattina et al. *Clin Transplant* 2012;26:910
• Cardiovascular disease
  – Incidence of severe CAD (> 70% stenosis) significantly higher is NAFLD (2% v 13%, \( p < 0.005 \))
  – Patients with more than one CV risk factor (male, age>50, smoking, hypercholesterolemia, DM) are at greater risk; consider coronary angiography
  – Diabetes can be associated with asymptomatic CAD; DM and CAD have poor prognosis after LTx
  – Dobutamine stress echocardiogram had poor predicative value for CAD in NAFLD patients
  – Prolonged QT interval – found in 77% of patient with NAFLD who experienced a CV event after LTx
Pre-Transplant Cardiac Evaluation

- EKG
  - Prolonged QT interval
    - after the 3rd beat
    - Consider hepatopulmonary syndrome
  - Early passage of bubbles to left cavities
    - before the 3rd beat
    - Transesophageal echocardiography
- Echocardiography (with bubbles if hypoxemia)
  - RSVP > 50 mmHg
  - LVEF < 50%
  - Right heart catheterization
    - CAD screening
      - Stress tests
      - TC calcification score
      - Coronary Angiography
Obesity and Liver Transplantation

• Dieting, medications, physical activity and behavioral therapy to address obesity prior to liver transplant rarely effective and poorly tolerated by debilitated patients

• Bariatric surgical options before, in conjunction with, or after transplantation (no randomized trials)
  – Sleeve gastrectomy
  – Gastric banding
  – Roux-en-Y gastric bypass
Types of Bariatric Surgery

Gastric Sleeve Surgery (Vertical Sleeve Gastrectomy)

Vertical Sleeve Gastrectomy

Gastric sleeve (new stomach)

Removed portion of stomach
Types of Bariatric Surgery

Adjustable Gastric Banding (Lap Band Surgery)

Adjustable Gastric Band (Lap Band)

Stomach pouch
Adjustable band
Port placed under skin
Types of Bariatric Surgery

Gastric Bypass Surgery (Roux-en-Y)

Roux-en-Y Gastric Bypass (RNY)

- Bypassed portion of stomach
- Gastric pouch
- Bypassed duodenum
- Jejunum

Duodenum

Jejunum

food

digestive juice
NAFLD & Waiting List Dynamics

- Studies have documented increased waiting list dropout, waitlist mortality and waitlist stagnation for patients with NAFLD.
- Lower rates of receiving LTx within 90 days of listing and lower 1-yr waitlist survival for those with NASH compared to ALD or HCV.
- Slower progression of disease in patients with NASH results in increased risk of death and removal from the wait list compared to HCV patients.
### Non-alcoholic Steatohepatitis

<table>
<thead>
<tr>
<th>Year Range</th>
<th>1-year</th>
<th>3-year</th>
<th>5-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002-2004</td>
<td>87.5%</td>
<td>80.7%</td>
<td>75.6%</td>
</tr>
<tr>
<td>2005-2007</td>
<td>86.7%</td>
<td>81.0%</td>
<td>75.5%</td>
</tr>
<tr>
<td>2008-2010</td>
<td>89.5%</td>
<td>82.5%</td>
<td></td>
</tr>
<tr>
<td>2011-2012</td>
<td>89.3%</td>
<td></td>
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</tr>
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</table>
NASH & Post-transplant Survival

- NASH vs controls (transplanted for other etiologies)
  - NASH patients were older, more often female, suffered from HTN and DM at time of LTx
  - 5-yr survival comparable to controls but tendency to higher 30-day and 1-yr mortality
  - Infection/sepsis most common cause of death
  - Pre-transplant renal failure and need for hemodialysis may predict reduce survival post-Tx

Agopian et al. *Ann Surg* 2012;256:624
NASH & Post-transplant Survival

• NASH vs controls (transplanted for other etiologies)
  – Increased risk of cardiac events including sudden cardiac death and acute heart failure within 1 yr of transplant
  – Renal dysfunction is an important predictor of CVD mortality in NASH patients
  – Overall excellent mid- and long-term patient and graft survival in patients transplant for NASH cirrhosis

Therapondos et al. Liver Transpl 2004;10:1441
VanWagner et al. Liver Int 2015;35:2575
NAFLD After Liver Transplantation
# Post-transplant Metabolic Syndrome

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pre-transplant</th>
<th>Post-transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>20% - 30%</td>
<td>30% - 70%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10% - 30%</td>
<td>61%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20% - 40% (de novo)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10%</td>
<td>62%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>3%</td>
<td>45%</td>
</tr>
</tbody>
</table>
## Immunosuppression Aggravates Metabolic Syndrome

<table>
<thead>
<tr>
<th>Immunosuppressant</th>
<th>Metabolic Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrolimus (Prograf)</td>
<td>Hypertension, Diabetes</td>
</tr>
<tr>
<td>Cyclosporine (Neoral)</td>
<td>Dyslipidemia, Hypertension</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Hypertension, Dyslipidemia, Diabetes</td>
</tr>
<tr>
<td>Sirolimus (Rapamune)</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Azathioprine (Imuran)</td>
<td>No significant effects</td>
</tr>
<tr>
<td>Mycophenolate mofetil (Cellcept)</td>
<td>No significant effects</td>
</tr>
</tbody>
</table>
Post-transplant NAFLD

• Two forms of NAFLD:
  – **Recurrent** NAFLD (30%-100%) – recurrent NASH in 4%-33%; risk of advanced fibrosis and cirrhosis is low
  – **De novo** NAFLD (18%-78%) due to increased risk factors such as dyslipidemia, hypertension and DM; de novo NASH in 5%-9%
  – Severe fibrosis and steatohepatitis more frequent in patients with recurrent NASH, but not a major concern for long-term patient and graft survival

Vallin et al. *Liver Transpl*;20:1064
Donor Steatosis
Donor Liver Steatosis
Risks of Donor Steatosis

Marsman et al. Transplantation 1996
NAFLD in the Donor Liver

- Steatotic livers may be considered “extended criteria donors” depending on the amount of fat present
- Steatosis >60% not transplanted
- Steatosis 30%-60% associated with poor results including decreased graft function, graft survival and patient survival
- Living donor transplant programs often exclude donors with >10% -15% macrovesicular steatosis
- Macrovesicular steatosis appears better than microvesicular steatosis
- Donor hepatic steatosis can disappear after transplant
Recommendations for Obese Patients Presenting for Liver Transplant

- Patients must have a “dry weight” BMI < 35 kg/m² before liver transplantation
- Decreased dietary carbohydrates and fats with relative preservation of protein to avoid muscle wasting
- Exercise for caloric utilization, muscle preservation and development of healthy lifestyle habits
- Modify immunosuppression to avoid metabolic complications after surgery
- Aggressive management of metabolic complications when they occur post-transplant
Mediterranean Diet

Food Guide Pyramid
A Guide to Daily Food Choices

- Fats, Oils, & Sweets
  Use Sparingly

- Milk, Yogurt, & Cheese Group
  2–3 Servings

- Vegetable Group
  3–5 Servings

- Meat, Poultry, Fish, Dry Beans, Eggs, & Nuts Group
  2–3 Servings

- Fruit Group
  2–4 Servings

- Bread, Cereal, Rice, & Pasta Group
  6–11 Servings

KEY
- Fat (naturally occurring and added)
- Sugars (added)

These symbols show that fat and added sugars come mostly from fats, oils, and sweets, but can be part of or added to foods from the other food groups as well.

SOURCE: U.S. Department of Agriculture/U.S. Department of Health and Human Services
Pharmacologic Interventions

- Metformin
- Pioglitazone
- Glucagon-like peptide-1 (GLP-1) agonists
- Dipeptidyl peptidase-4 (DPP-1) inhibitors
- Pentoxifylline
- Statins
- Ezetimibe
- Fibrates
- Niacin
- Vitamin E
Targets Used for Treatment of NAFLD/NASH

- OCA
- Ezetimibe
- Aramchol
- Elafibranor (GFT505)

Dyslipidemia → NAFLD → Obesity

Insulin Resistance → NAFLD

Oxidative Stress → NASH

Fibrosis → Liver-related outcomes

Proinflammatory Pathways

GS-4997
Cenicriviroc
GR-MD-02

Abbreviations: NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; OCA, obeticholic acid.