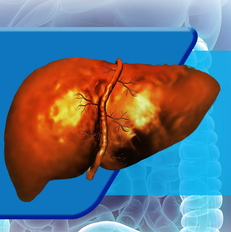
Guidelines at a Glance:

Contemporary Recommendations for the Use of Disease-Specific MASH Treatments



Treatment of MASH includes comprehensive lifestyle modifications (nutrition, exercise, and behavior modification) and optimal control of comorbid conditions. Some patients may benefit from MASH-specific therapy to improve outcomes.

EASL-EASD-EASO Guidelines for Therapeutic MASH Management

Preferred pharmacologic options for treating comorbidities

	MASH-targeted	T2D	Dyslipidemia	Obesity
MASLD/ MASH without cirrhosis (F0-F3)	*If locally approved:* **Resmetirom** in F2/F3 fibrosis	**GLP-1RA** (eg, semaglutide, liraglutide, dulaglutide) and coagonists (eg, tirzepatide) **SGLT2 inhibitors** (eg, empagliflozin, dapagliflozin) **Metformin**[a] **Insulin** (in case of decompensated cirrhosis)	**Statins**	**GLP-1RA** (eg, semaglutide, liraglutide, dulaglutide) and coagonists (eg, tirzepatide) **Bariatric interventions** (special caution in case of compensated cirrhosis)
MASLD/ MASH with compensated cirrhosis (F4)	Check indication for liver transplantation in case of decompensation or HCC			

[a]If glomerular filtration rate is >30 mL/min.

Patient Selection for Resmetirom Therapy

Expert Consensus

MASLD

Assess steatosis
Rule out other causes of liver disease

Treat	Consider treatment	Do not treat
VCTE ≥10-15 kPa **OR** MRE ≥3.3-4.2 kPa **OR** ELF score 9.2-10.4 kPa **OR** FAST, MAST, MEFIB **AND** platelets ≥140 k/µL **AND** no evidence of PHTN	VCTE 15.1-19.9 kPa **OR** MRE 4.3-4.9 kPa **OR** ELF score 10.5-11.3 kPa **OR** FAST, MAST, MEFIB **AND** platelets ≥140 k/µL **AND** no evidence of PHTN	VCTE ≥20 kPa[a] **OR** MRE ≥5 kPa[a] **OR** ELF score >11.3[a]

[a]If biopsy is performed and liver histology demonstrates Stage 2 or 3 disease, treatment is appropriate, as long as there is no clinical or imaging evidence of PHTN (eg, ascites apparent on imaging, gastroesophageal varices, history of hepatic encephalopathy).

AASLD Guidance

Not recommended
- Cirrhosis, including LSM via VCTE >20 kPa or MRE >5 kPa
- Concomitant active liver disease
- Excess alcohol use (>20/30 g/d in women/men)
- Active thyroid disease

Recommended

Imaging-based NILDA	VCTE: LSM 8-15 kPa[a] MRE: LSM 3.1-4.4 kPa[a]
Liver histology	MASH with F2-F3[b]

May be used
- Individualized decisions by a specialist experienced in liver fibrosis for:
  - LSM values outside the recommended ranges
  - Other NILDA data consistent with F2-F3[c]

[a]Modified from the AASLD NILDA guidelines.
[b]Liver biopsy is not routinely recommended for staging of MASH.
[c]Imaging-based NILDA is preferred (eg, shear wave elastography [applying local standards for F2-F3]) vs ELF score (9.2-10.4). The latter range is based on the IQR from the MAESTRO trial data; no recommendations are available from the AASLD NILDA guidelines.

Resmetirom Treatment Monitoring

Expert Consensus

Assess safety and efficacy at 12 months

Worsening of NITs[a] → **STOP**

No change in NITs[a] → **Consider continuing, add-on, or alternative approach**

Assess treatment response
- **ALT** >17 IU/L and/or >20% improvement[c] or normalization
- **VCTE** ≥30% drop in LSM
- **MRI-PDFF** ≥30% in liver fat

→ **Continue**

Monitor for safety at 3, 6, and 12 months

[a]ALT improvement should be accompanied by improvement in imaging (≥30% reduction in MRI-PDFF). If no improvement in ALT, ≥30% reduction in PDFF can still be predictive of response. VCTE alone may be inadequate to assess treatment response. Based on MAESTRO NASH, histologic improvements may occur without corresponding changes in VCTE or liver enzymes, emphasizing the importance of considering MRI-PDFF or liver biopsy before labeling patients as unresponsive to treatment.

AASLD Guidance

Response assessment at 12 months

• Worsening of NILDA[a] • Consistent increase in ALT	No response	**Stop resmetirom**
• Improvement in LSM (kPa)[b] by VCTE ≥25% or MRE ≥20% from baseline • Normalization or significant improvement in ALT[c]	Beneficial response	**Continue resmetirom**
• Minor reduction in LSM (kPA)[b] VCTE <25% or MRE <20% from baseline • No significant improvement in ALT[c] • <30% reduction in MRI-PDFF[d]	Benefit uncertain	**Re-evaluate strategy[e]**

Monitor for safety at 3, 6, and 12 months

[a]Assess based on the same imaging-based or blood-based markers used to determine treatment eligibility.
[b]LSM improvement thresholds of VCTE ≥25% or MRE ≥20% are based on assay characteristics and not specifically validated for clinical decisions in resmetirom treatment patients. There are currently no comparable data to determine response in blood-based NILDAs.
[c]Applies to patients with elevated ALT at baseline. No specific ALT response cutoffs are available from the MAESTRO trial.
[d]MRI-PDFF reduction by >30% does not necessarily correlate with histologic response.
[e]Options may include re-optimizing lifestyle interventions and considering other therapy, with or without stopping resmetirom.

Abbreviations

AASLD: American Association for the Study of Liver Diseases
ALT: alanine aminotransferase
EASL: European Association for the Study of the Liver
EASD: European Association for the Study of Diabetes
EASO: European Association for the Study of Obesity
ELF: enhanced liver fibrosis
FAST: FibroScan-Aspartate Aminotransferase
GLP-1RA: glucagon-like peptide-1 receptor agonist
HCC: hepatocellular carcinoma
IQR: interquartile range
LSM: liver stiffness measurement
MASH: metabolic dysfunction-associated steatohepatitis
MASLD: metabolic dysfunction-associated steatotic liver disease
MAST: magnetic resonance imaging AST
MEFIB: MRE combined with Fibrosis-4
MRE: magnetic resonance elastography
MRI-PDFF: magnetic resonance imaging proton density fat fraction
NILDA: noninvasive liver disease assessment
NIT: noninvasive test
PHTN: portal hypertension
SGLT2: sodium-glucose cotransporter 2
T2D: type 2 diabetes
VCTE: vibration-controlled transient elastography

References

Chen VL, et al. *Hepatology.* 2025;81:312-320.
EASL-EASD-EASO. *Diabetologia.* 2024;67:2375-2392.
Noureddin M, et al. *Clin Gastroenterol Hepatol.* 2024;22:2367-2377.