The Emoroid Digest

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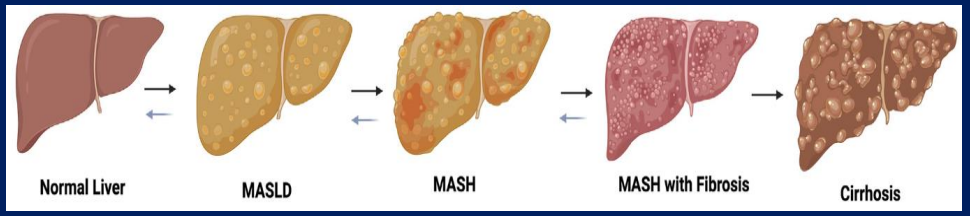
Emory Faculty Retroflexions: New Treatment Options for MASLD/MASH

Hayalneh Gessessew, MD in Discussion with Ravi Vora, MD

Pathophysiology



Fat accumulation > Inflammation > Fibrosis

Abushamat et al. (2024) the emerging role of glucagonlike peptide-1 receptor agonists in treating metabolic dysfunctionassociated steatohepatitis https://www.mashclinical.com/what-is-mash

Available Treatment Options

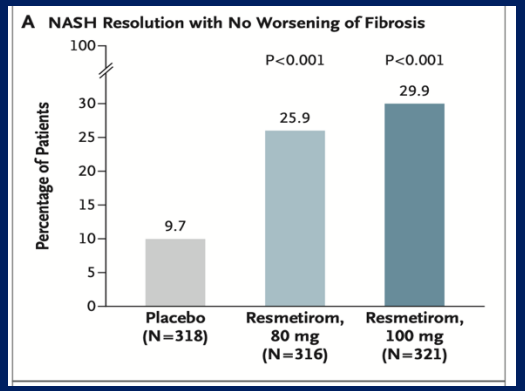
Medication	Mode of Action	Adverse Reaction
Resmetirom **Only current FDA approved therapy	Activates THR-Beta, enhancing lipid metabolism and reducing hepatic fat.	N/V/D, changes in thyroid hormone levels
GLP-1 RA	Improves insulin resistance, reduces hepatic lipogenesis, anti-inflammatory, weight loss	Nausea, vomiting, diarrhea, pancreatitis
Pioglitazone	Activates PPAR-γ, enhancing insulin sensitivity & reducing hepatic fat accumulation	Weight gain, Edema
Vitamin E	Reduces oxidative stress & inflammation in the liver	Hemorrhagic stroke, prostate cancer risks

https://www.aasld.org/liver-fellow-network/core-series/backbasics/treatticliver-disease-cutting-through-fat

"MASLD is a systemic disease, & in my practice, I advocate for co-management with PCP, cardiology, and endocrinology. I try to anchor liver health in the broader context of metabolic health to improve patient buy-in. We're moving toward integrated clinics, where MASLD is managed with unified care pathways."

Resmetirom

- FDA approved in 2024 w clinical trials showing resolution in MASH & improvement in liver fibrosis by at least 1 stage (figure A below)
- For adults with MASH/MALD & F2-F3 disease, diagnosed on non-invasive measurements or liver biopsy
- Dosage: 100 mg for patients >100 kg, or 80 mg for patients <100 kg

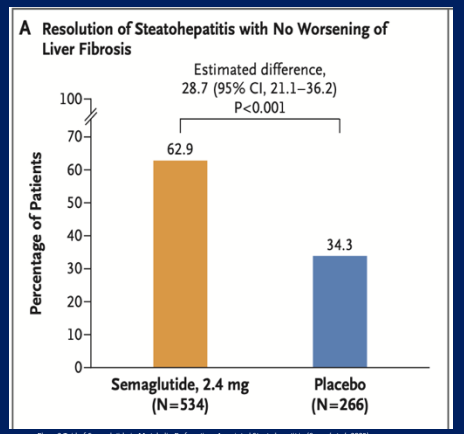


A Phase 3,Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis, (S.A. Harrison et al.2024)

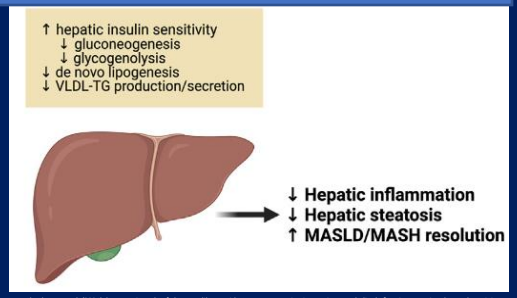
"As hepatologists, we are transitioning from supportive care toward evidence-based, targeted therapies supported by a multidisciplinary and precision medicine approach. The coming decade will redefine how we think about fatty liver as a cardiometabolic risk amplifier worthy of proactive and aggressive management."

GLP-1 Receptor Agonists

- Initially considered for intermediate to high-risk patients w MASH or MASLD, who also have 1) BMI >27 with >2 obesity related conditions, 2) BMI >30, or 3) Type 2 DM



Phase3 Trial of Semaglutide in Metabolic Dysfunction–Associated Steatohepatitis (Sanyal et al. 2025)



Abushamat et al. (2024) the emerging role of glucagon-like peptide-1 receptor agonists in treating metabolic dysfunction-associated steatohepatitis

- In recent phase 3 clinical trial (April 2025), once-weekly 2.4 mg improved liver histologic results in patients with MASH / MASLD after 72 weeks.
- Study population: patients w/ biopsy-defined MASH and fibrosis stage 2 or 3
- Semaglutide showing resolution of steatohepatitis (left fig. A) as well as improvement of fibrosis by at least 1 stage
- Not yet FDA approved

Future Directions

- **Analogs of fibroblast growth factors:** phase 2 trials showing it may improve liver fat reduction, fibrosis, and inflammation
- **GLP-1/Glucagon Dual receptor agonists:** glucagon receptor agonism helps increase hepatic energy expenditure and promote lipolysis

"The approval of resmetirom marks a turning point. Weight loss medications like GLP-1 receptor agonists are already showing promise in reversing steatosis and improving histology. Future trials will involve combination therapies—targeting metabolic, inflammatory, and fibrotic pathways simultaneously."