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Summary

What's the best approach to lifestyle change and which drugs are likely to be approved for MASH therapy?

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Education & Training | Hepatobiliary | Primary Care

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Combined lifestyle intervention targeting weight loss remains the cornerstone of MASH management across all disease stages, while emerging pharmacotherapies including thyroid hormone receptor beta agonists, incretin mimetics, and FGF21 analogues show promise for fibrosis regression in clinical trials.

KEY POINTS

- The speaker reported that a 12-week high-intensity interval exercise intervention in 15 MASH patients improved cardiorespiratory fitness and muscle metabolism but produced no significant change in liver parameters when weight remained stable, suggesting weight loss rather than exercise alone drives hepatic benefit.
- Meta-analysis of dietary studies showed hypocaloric and Mediterranean diets achieved 2.2 to 2.9 kg weight loss on average, with steatosis regression demonstrated by ultrasound but no data on fibrosis or steatohepatitis outcomes.
- The speaker stated that combined lifestyle interventions in the Vilar-Gomez and BRAVES trials demonstrated histological improvement proportional to weight loss, with the BRAVES lifestyle arm also permitting vitamin E and incretin use.
- Resmetirom, a thyroid hormone receptor beta agonist approved by FDA in March 2024, showed 12% fibrosis improvement over placebo at one year in a phase 3 trial, representing what the speaker called a dramatic effect given fibrosis changes slowly.
- Phase 2 data presented for survodutide, a GLP-1 and glucagon receptor agonist with direct liver effects, showed 40% improvement over placebo in the high-dose group, the largest delta the speaker reported seeing in the field for this endpoint.

- The speaker stated that bariatric surgery has strong evidence including in compensated cirrhosis but remains invasive and underused, while acknowledging that GLP-1 agonist adherence data suggest 50 to 70% discontinuation by one to two years with subsequent weight regain.

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