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Summary

Targeting the liver: Effects beyond obesity

Naim Alkhouri

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Hepatobiliary | Small Intestine & Nutrition | Mechanisms & Personalised Medicine

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The speaker presented liver-directed therapies for NASH, highlighting that resmetirom (thyroid hormone receptor beta agonist) and dual/triple incretin agonists targeting glucagon can improve liver fat, inflammation, and fibrosis through mechanisms beyond weight loss.

KEY POINTS

- The speaker reported that in the Maestro NASH phase 3 trial, resmetirom achieved NASH resolution in up to 30% of patients and fibrosis improvement in up to 26% of patients with F2-F3 fibrosis treated for 52 weeks, with the drug receiving FDA and EMA approval in 2024.
- Resmetirom targets thyroid hormone receptor beta selectively in the liver, increasing fatty acid oxidation and mitophagy while reducing LDL cholesterol and atherogenic lipids, according to the speaker.
- The speaker stated that survodutide, a GLP-1 and glucagon dual agonist, showed fibrosis improvement with up to 30% delta from placebo in a 48-week study, with mediation analysis indicating fibrosis benefits were mainly weight loss independent.
- In the SYNCHRONIZE-NAFLD phase 3 study, the speaker reported that close to 85% of patients treated with survodutide achieved at least 30% relative reduction in liver fat and 61% normalized liver fat to less than 5%.
- The speaker noted that resmetirom can be safely combined with GLP-1 agents without drug-drug interactions, as demonstrated in Maestro NASH where up to 15% of patients were on stable-dose GLP-1 therapy.
- The speaker recommended that both liver specialists and endocrinologists should be comfortable prescribing these therapies and monitoring multiple organ systems in patients with metabolic disease.

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