The best approach to NASH is to treat the root cause rather than a pure anti-fibrotic strategy

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## Conflict of interest disclosure

<table>
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The best approach to NASH is to treat the root cause rather than a pure anti-fibrotic strategy.
3 Reasons

• Why do patients with NASH die?

• Directly acting anti-fibrotic therapies unlikely to work well by themselves

• Treating the cause of a problem is the only way
What do patients with NASH die from?

619 patients with bx-confirmed NAFLD 1975-2005

US, Europe & Thailand

12.6 years f/u (range 0.3-35.1)

Angulo et al, Gastro 2015
Not much liver-related mortality...

Taylor et al. Gastro 2020
3 Reasons

• Why do patients with NASH die?

• Directly acting anti-fibrotic therapies unlikely to work well by themselves

• Treating the cause of a problem is the only way
Directly acting anti-fibrotic therapies don’t work (by themselves)

Harrison et al. Gastro 2018
Directly acting anti-fibrotic therapies don’t work (by themselves)

Harrison et al, J Hepatol 2020
3 Reasons

• Why do patients with NASH die?

• Directly acting anti-fibrotic therapies unlikely to work well by themselves

• Treating the cause of a problem is the only way
Treating the cause of a problem works in Hep B

Regression of cirrhosis during treatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study

And also in NASH...

Lifestyle intervention reduces portal pressure in overweight patients with liver cirrhosis & portal hypertension

Berzigotti A et al. Hepatology. 2017

**Trial information**
- 16-week **lifestyle intervention**
- 60 patients with compensated cirrhosis and portal hypertension
  - **Age**: 56 years
  - NASH aetiology: 24%
  - **BMI**: 33.3 kg/m²
  - **HVPG ≥10 mmHg**: 72%

**Results after lifestyle intervention**
- **BW**: ~5.0 kg
  - ≥5% reduction: 52%
  - ≥10% reduction: 16%

- **HVPG**: 13.9 to 12.3 mmHg**
  - ≥10% reduction: 42%
  - ≥20% reduction: 24%

- ≥10% BW loss associated with a greater decrease in HVPG (~23.7% vs ~8.2%*)
And has impacts beyond the liver
Conclusion

Reasons

• Patients with NASH don’t just die from liver disease

• Directly acting anti-fibrotic therapies not likely to work well when used alone

• Treating the cause of a problem makes sense and actually works!