Baseline ANTICIPATE score and response predicts liver outcome events in a 180 patient MASH cirrhosis cohort treated with resmetirom

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INTRODUCTION

- Resmetirom, a selective thyroid hormone receptor β agonist, indicated in conjunction with diet and exercise for the treatment of metabolic dysfunction–associated steatohepatitis (MASH) with moderate to advanced fibrosis (consistent with fibrosis stages F2 to F3), based on histological improvements in steatohepatitis and fibrosis[1,2]
- Patients with compensated MASH cirrhosis remain at risk of clinically significant portal hypertension (CSPH) and subsequent liver-related events (LREs),[3] highlighting the need for tools that can stratify risk and monitor treatment response
- ANTICIPATE-NASH is a noninvasive model incorporating body mass index (BMI), platelet count and liver stiffness to estimate CSPH risk and predict clinical outcomes.[4] The score predicts the likelihood of experiencing an LRE in the subsequent 3 years, <25% (score <0.25) is associated with a low likelihood of events, whereas >75% (>0.75) is associated with a high likelihood of decompensation events.
- Its utility in patients receiving disease-modifying therapy such as resmetirom has not been fully characterised

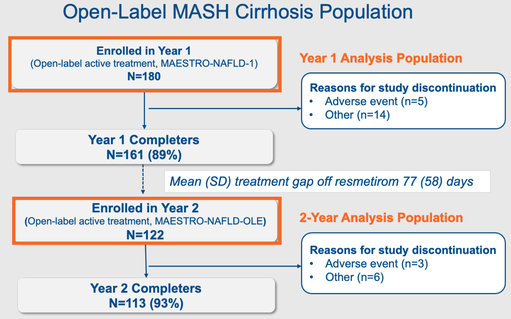
AIM

- To evaluate whether the ANTICIPATE-NASH score predicts CSPH risk and LREs in patients with compensated MASH cirrhosis treated with resmetirom for up to 2 years

METHODS

- Study design
  - This analysis included patients with well-compensated MASH cirrhosis enrolled in MAESTRO-NAFLD-1 (NCT04197479) and its open-label extension (OLE) study (NCT04951219), who received resmetirom 80 mg for 2 years
- Study population
  - This study included adults with compensated MASH cirrhosis (Child-Pugh class A) and no history of decompensation events
  - Cirrhosis was defined by historical biopsy-confirmed fibrosis stage F4 disease or clinical diagnosis; >66% of patients had biopsy-confirmed cirrhosis
  - Of the 180 patients included in the Year 1 analysis, 122 elected to enter the OLE and were included in the Year 2 analysis (**Figure 1**)
  - Discontinuation rates were <10% per year

Figure 1. Analysis population and follow-up through 2 years



CSPH, clinically significant portal hypertension; LRE, liver-related event.

- Baseline characteristics
  - Baseline demographics and clinical characteristics included age, sex, body mass index, type 2 diabetes status, noninvasive liver assessments (vibration-controlled transient elastography, magnetic resonance elastography) and platelet count
- Outcomes
  - Change in ANTICIPATE-NASH CSPH risk categories over time (baseline, Year 1, Year 2)
  - Responder status, defined as a shift to a lower category of ANTICIPATE-NASH which is scored in 25% increments.
  - Incidence of LREs at Year 1 and Year 2
  - Analyses were descriptive; no formal hypothesis testing was performed

RESULTS

- Patient characteristics
  - Baseline characteristics were generally similar between the Year 1 total population (MAESTRO-NAFLD-1) (n = 180) and the Year 2 population that enrolled for a second year (n = 122) populations (**Table 1**). The subpopulations according to baseline platelet count were evaluated.

TABLE 1. Baseline demographic and clinical characteristics

Characteristic	Year 1-all patients n = 180	2-Year Population n = 122	Platelets <100K n = 30	Platelets ≥100K n = 92
Age (years), median (IQR)	62.0 (56.0, 68.0)	62.0 (57.0, 68.0)	60.5 (56.0, 66.0)	62.0 (57.0, 68.5)
Female, %	112 (62.2%)	68 (55.7%)	14 (46.7%)	54 (58.7%)
BMI (kg/m^2), median (IQR)	34.4 (30.6, 38.9)	34.4 (30.6, 38.9)	35.1 (32.7, 38.9)	33.4 (30.2, 39.0)
T2D, %	131 (72.8%)	85 (69.7%)	22 (73.3%)	63 (68.5%)
LSM by VCTE (kPa), median (IQR)	20.3 (15.6, 30.7)	20.1 (17.1, 31.3)	26.4 (17.7, 39.6)	19.3 (16.1, 27.4)
LSM by MRE (kPa), median (IQR)	5.1 (4.1, 6.3)	5.2 (4.4, 6.3)	5.9 (4.9, 6.7)	5.1 (4.0, 5.9)
Platelets (10^9/L), median (IQR)	142 (108, 199)	136 (101, 187)	89 (77, 91)	156 (128, 208)
ANTICIPATE-NASH Score, median (IQR)	0.37 (0.20, 0.67)	0.45 (0.25, 0.70)	0.72 (0.55, 0.89)	0.34 (0.15, 0.59)

BMI, body mass index; kPa, kilopascal; IQR: interquartile range; LSM, liver stiffness measurement; MRE, magnetic resonance elastography; Q, quartile; T2D, type 2 diabetes; VCTE, vibration-controlled transient elastography.

- CSPH risk distribution over time
  - In the 2 Year analysis population, the proportion of patients with high CSPH risk (>25%) decreased progressively from 75% at baseline to 60.3% at Year 1 and 54.5% at Year 2 (**Figure 2**)
  - These findings indicate a sustained reduction in portal hypertension risk over time
  - The distribution shifted toward lower-risk categories, with increases observed low-risk (≤25%) groups over time, and decreases observed in higher risk groups (>50%) reflecting overall improvement in CSPH risk profiles

Figure 2. Distribution of ANTICIPATE-NASH risk categories at baseline, Year 1, Year 2

- Treatment response
  - The geometric mean ANTICIPATE-NASH score declined by 27.1% in the one-year MAESTRO-NAFLD-1 population, 25.5% and 37.6% at years 1 and 2 in the 2-Year analysis population (**Figure 3**)
  - The increase in patients with scores ≤25% was 58.6% after one year

Figure 3. % Change in ANTICIPATE-NASH

DISCLOSURES

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- Liver-related events (LRE)
  - LREs occurred primarily in patients with baseline platelets <100K (7/8)
  - BMI did not show a relationship to LRE
  - LREs were infrequent and occurred only in patients with baseline CSPH risk >25% (**Figures 4, 5**)

Figure 4. Incidence of LREs at Year 1 in the overall (n=180) Cohort and the second year of the 2-Year population (n=122) according to baseline BMI and baseline ANTICIPATE-NASH score

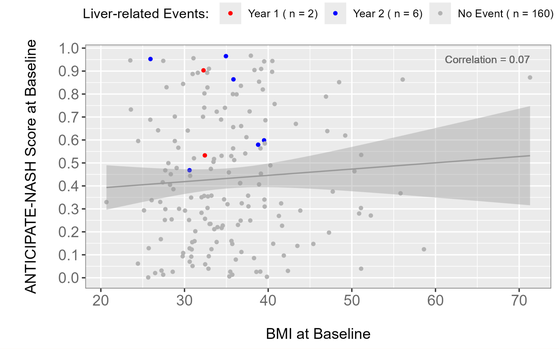
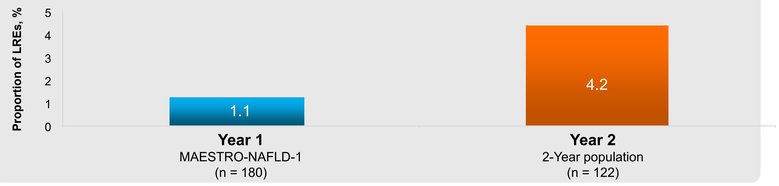


Figure 5. Incidence of LREs at Year 1 in MAESTRO-NAFLD-1 Cohort and the second year of the 2-Year population



LRE, liver-related event. LRE rate was estimated based on Fine-Gray method with deaths treated as competing risk. Event rate was assessed only in the second year of treatment (Year 1 to Year 2) independent of Year 1 in the 2-Year population as an event in year one was an exclusion for entering Year 2.

CONCLUSION

- **ANTICIPATE-NASH stratifies CSPH risk in patients treated with resmetirom for compensated MASH cirrhosis**
- **Approximately half of patients demonstrated meaningful improvement in CSPH risk with resmetirom treatment**
- **LREs were rare and occurred exclusively in high-risk patients with CSPH risk >25%**
- **These findings suggest ANTICIPATE-NASH may serve as a clinically actionable tool to guide risk stratification and monitoring in patients receiving disease-modifying therapy**

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REFERENCES

1. Rezdiffra (resmetirom) tablets, for oral use. Prescribing information. Madrigal Pharmaceuticals, Inc.; 2025. **2.** Harrison SA et al. *N Engl J Med*. 2024;390(6):497-509. **3.** Paternostro R et al. *J Hepatol*. 2024;81(5):827-836. **4.** Aceituno L et al. *Gastroenterology*. 2026;170(2):385-394. **5.** Harrison SA et al. *Nat Med*. 2023;29(11):2919-2928. **6.** Harrison SA et al. *Aliment Pharmacol Ther*. 2024;59(1):51-63.