A nonalcoholic steatohepatitis (NASH) fibrosis and resolution cost-effectiveness model comparing resmetirom to standard of care in the United States

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BACKGROUND

- Nonalcoholic Steatohepatitis (NASH; also known as metabolic dysfunction-associated steatohepatitis or MASH) is associated with an accelerated progression toward cirrhotic NASH and advanced liver diseases
- Resmetirom was conditionally approved in the United States (US) as treatment for adults with Noncirrhotic NASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis)

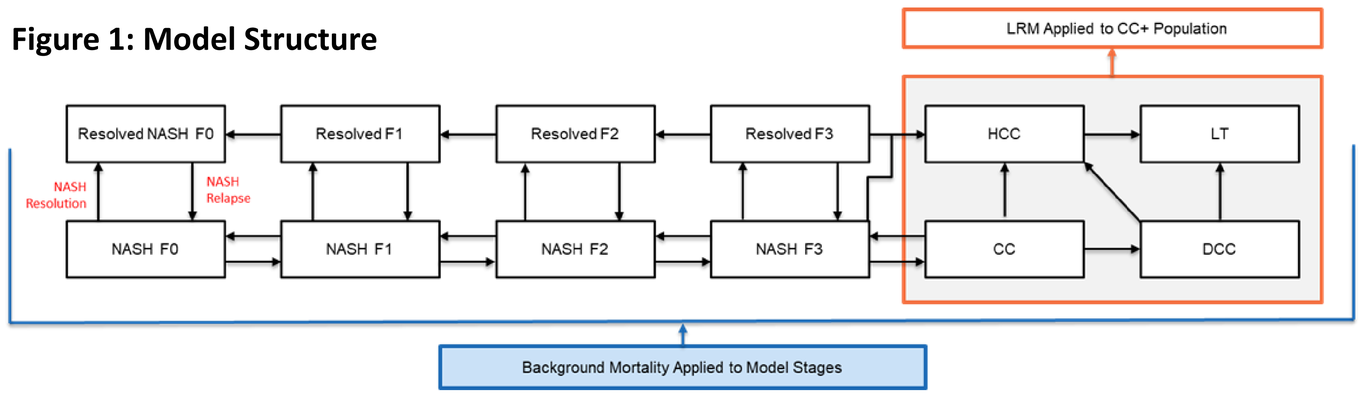
OBJECTIVE

- Assess the cost-effectiveness of resmetirom compared to standard-of-care (SOC) for NASH resolution and fibrosis improvement from the perspective of US private payers

METHODS

- A health state transition model was developed to reflect the clinical pathways of patients who are treated for NASH at fibrosis stages F2 or F3
- Population included adult patients ≥18 years of age (average: 57) with NASH and liver fibrosis in alignment with the MAESTRO NASH phase III trial
- The model structure allowed for transitions to fibrosis improvement or worsening, with or without NASH resolution (Figure 1)
- Noncirrhotic state transition probabilities were based on published estimates and the placebo arm from the MAESTRO-NASH phase III trial
- Health utilities, direct medical costs and transition probabilities to compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and liver transplant were collected from published literature
- The comparator was standard of care including diet and exercise (no other drug therapies are approved for the treatment of NASH with significant fibrosis)
- The intervention was 100 mg or 80 mg resmetirom in a once-daily oral tablet
- The resmetirom treatment effect for progression, regression, and NASH resolution, discontinuation, adverse events rates, and noncirrhotic health utilities were estimated from MAESTRO-NASH data
- Direct medical costs and QALYs were discounted at 3 percent annually
- Deterministic and probabilistic sensitivity analysis (DSA, PSA) assessed model uncertainty
- Outcomes relevant for a private payer were calculated over a lifetime (50 years) with 1-year model cycles
- Mortality outcomes for the model's SOC-arm were compared to ten-year mortality from a recent systematic literature review (Ng et al., 2023)

Figure 1: Model Structure



Notes: NASH: Non-alcoholic steatohepatitis, NAFLD: Non-alcoholic fatty liver disease, F0-F3: Fibrosis stage (F0-F3), LT: Liver transplant, CC: Compensated cirrhosis, DCC: Decompensated cirrhosis, HCC: Hepatocellular carcinoma, LRM: Liver-related mortality.

RESULTS

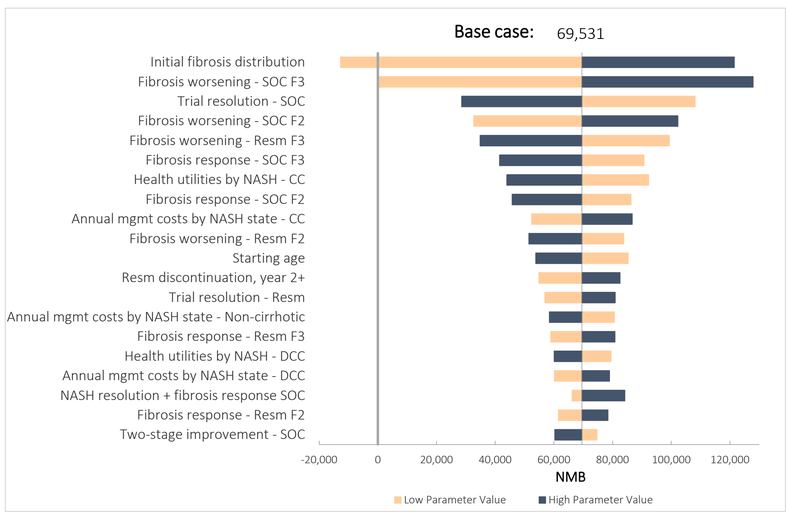
- Resmetirom reduced DCC, HCC and LT by 39.2%, 8.3%, and 1.9% respectively compared to SOC over a lifetime horizon
- Base case lifetime costs and QALYs for resmetirom and SOC were respectively: $794,753 vs. $580,805 and 11.91 vs. 10.02 QALYs
- The incremental cost-effectiveness ratio (ICER) was $113,391 per QALY in the base case (Table 1)
- Assuming a willingness-to-pay (WTP) of $150K per QALY, resmetirom generated a net monetary benefit (NMB) of $69,075
- The DSA scenarios generated a positive NMB, with sensitivity to initial fibrosis distribution and the rate of SOC fibrosis worsening (Figure 2)
- Resmetirom was cost-effective versus SOC in 89.2% of the simulations at a WTP of $150K per QALY in the PSA (Figure 3)

Table 1: Base Case Results

	Resmetirom Blended	SOC	Δ / Difference
Detailed clinical incidence			
50-year CC incidence	39.18%	68.81%	-29.64%
50-year DCC incidence	12.35%	22.60%	-10.26%
50-year HCC incidence	8.30%	15.29%	-6.99%
50-year LT incidence	1.88%	3.50%	-1.62%
Liver-related mortality	25.24%	46.57%	-21.33%
Model Results (Discounted Lifetime Values)			
Direct medical costs ($)	794,753	580,805	213,948
QALYs	11.91	10.02	1.89
Life-years	14.42	12.56	1.86
ICER	-	-	113,391/QALY
NMB	-	-	$69,075

Notes: NASH: Non-alcoholic steatohepatitis, LT: Liver transplant, CC: Compensated cirrhosis, DCC: Decompensated cirrhosis, HCC: Hepatocellular carcinoma, ICER: Incremental cost-effectiveness ratio, LRM: Liver-related mortality, NMB: Net monetary benefit, QALY: Quality-adjusted life year, SOC: Standard-of-care

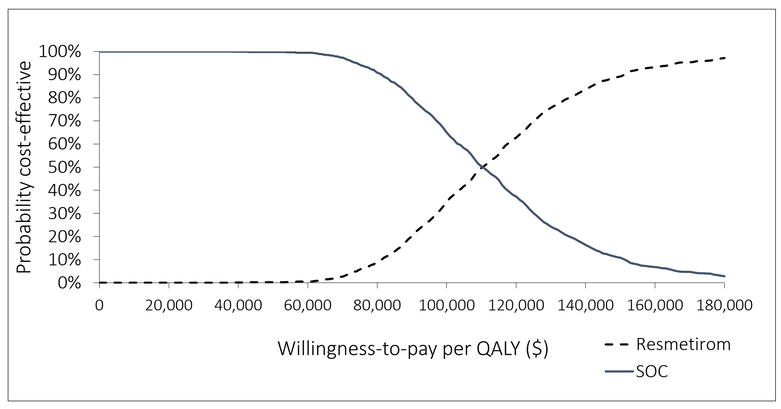
Figure 2: Deterministic Sensitivity Analysis on Net Monetary Benefit



Notes: NASH: Non-alcoholic steatohepatitis, NMB: Net monetary benefit, F0-F3: Fibrosis stage (F0-F3), CC: Compensated cirrhosis, DCC: Decompensated cirrhosis, SOC: Standard of care, Resm: Resmetirom

- A majority of simulations indicated that resmetirom was cost-effective at a WTP per QALY of $111,000 or higher
- The model predicted 34.1% mortality at 10 years for patients starting at F3 (Figure 4)

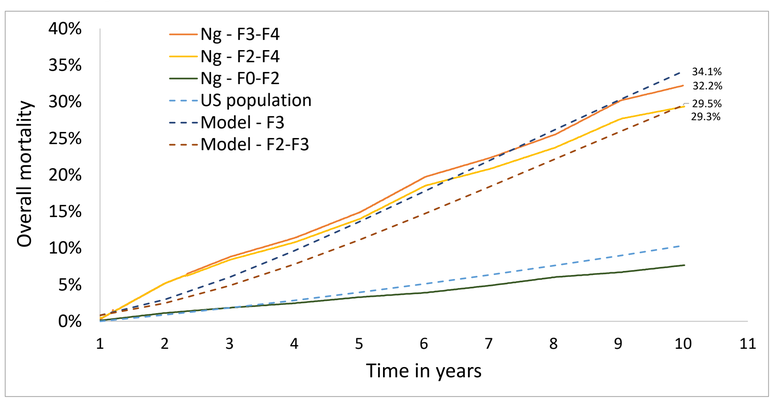
Figure 3: Cost-Effectiveness Acceptability Curve



Notes: SOC: standard-of-care, QALY: Quality-adjusted life-year

- In a systematic literature review (SLR; Ng et al., 2023), patients starting in either F3 or F4 experienced 32.2% mortality at 10 years
- Similarly, for simulated patients initiating the model in F2-F3 versus systematic literature review patients starting in F2-F4, 10-year mortality was 29.3% and 29.5% respectively (Figure 4)

Figure 4. SOC-arm Mortality Prediction Compared to SLR Mortality Prediction



Notes: F0-F3: Fibrosis stage (F0-F3)

DISCUSSION

- Model results indicated that although resmetirom increased direct medical costs, it improved quality-of-life and reduced rates of advanced liver disease in adult patients with noncirrhotic NASH and moderate-to-advanced liver fibrosis over a lifetime horizon
- Resmetirom demonstrated statistically significant evidence of improvements versus SOC in LDL cholesterol, apolipoprotein B, and triglycerides, among other hepatic endpoints; however, these effects were excluded from the model

CONCLUSION

- Resmetirom was a cost-effective treatment option compared to SOC at a WTP threshold of $110,000/QALY in adult patients with noncirrhotic NASH and moderate-to-advanced liver fibrosis
- The model was well-calibrated to approximate closely mortality in a recent SLR
- This economic analysis is focused on the U.S. and accordingly uses U.S. costs and pricing; costs and pricing for international countries have not been established

REFERENCES

1. Harrison et al. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. New England Journal of Medicine. 2024 Feb 8;390(6):497-509.
2. Chhatwal et al. Analysis of a Simulation Model to Estimate Long-term Outcomes in Patients with Nonalcoholic Fatty Liver Disease. JAMA Netw Open. 2022 Sep 1;5(9):e2230426.
3. Chong et al. Health-state utilities and quality of life in hepatitis C patients. The American journal of gastroenterology. 2003;98(3):630-8.
4. Morales et al. Immunosuppressant treatment adherence, barriers to adherence and quality of life in renal and liver transplant recipients in Spain. Clinical transplantation. 2012;26(2):369-76.
5. Tapper et al. Healthcare resource utilization and costs of care in the United States for patients with non-alcoholic steatohepatitis. Journal of medical economics. 2023;26(1):348-56.
6. Javanbakht et al. Early Cost-Effectiveness and Price Threshold Analyses of Resmetirom: An Investigational Treatment for Management of Nonalcoholic Steatohepatitis. Pharmacoecon Open. 2022
7. Neumann et al. Cost-effectiveness in health and medicine. Second ed. New York: Oxford University Press; 2017.
8. Younossi et al. SAT-459 Assessments of health utilities in patients with metabolic dysfunction-associated steatohepatitis (MASH): cross-walk between CLDQ-NASH, SF-6D, and the EuroQol EQ-5D. Journal of Hepatology. 2024 Jun 1;80:S652.
9. Ng et al. Mortality Outcomes by Fibrosis Stage in Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-analysis. Clinical gastroenterology and hepatology. 2023;21(4):931-9.e5

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DISCLOSURES

Design, study conduct, and financial support for the study were provided by Madrigal Pharmaceuticals, Inc.. Yestle Kim is employed by Madrigal Pharmaceuticals, Inc and may own stocks/and or options from Madrigal Pharmaceuticals, Inc. Dominic Mitchell, Hélène Parisé, and Scott Johnson are employees of Medicus Economics, LLC. Medicus Economics, LLC received consulting fees for research from Madrigal Pharmaceuticals, Inc. Zackary Smith was an employee of Medicus Economics, LLC at the time of development of the model. Medicus Economics, LLC received consulting fees for research from Madrigal Pharmaceuticals, Inc.