# The Impact of Treatment-related Changes in Lipids on the Cost-effectiveness of Resmetirom and Obeticholic Acid for Treatment of Nonalcoholic Steatohepatitis

**Amir Ansaripour[1], Jesse Fishman[2], Eoin Moloney[3], Mehdi Javanbakht[3]**

[1]Optimax Access Ltd, Hofplein, Rotterdam, The Netherlands; [2]Madrigal Pharmaceuticals, Conshohocken, PA; [3]Optimax Access Ltd, University of Southampton Science Park, Chilworth, Hampshire, UK

## BACKGROUND

- Lipid levels impact cardiovascular (CV) disease (CVD) risk, including myocardial infarction (MI) and stroke

## OBJECTIVE

- To assess the impact of treatment-related changes in lipid levels resulting from two potential treatments for nonalcoholic steatohepatitis (NASH) (resmetirom and obeticholic acid [OCA]) on costs and health outcomes versus placebo from a US healthcare payer perspective over a lifetime horizon

## METHODS

- We used a previously developed cost-effectiveness model which was composed of two submodels ('no prior CV event' and 'prior CV event') with equivalent liver disease-specific state transition probabilities to account for the occurrence of MI and stroke
- In each submodel, patients transitioned among no-fibrosis (F0) and fibrosis (F1-F3) stages, compensated cirrhosis (or F4), decompensated cirrhosis, hepatocellular carcinoma, post-liver transplant, and death. The transition from the first to second submodel was driven by the first occurrence of a nonfatal CV event, estimated based on pooled baseline characteristics[1]
- Data on the 10-year CV risk were calculated using the Framingham CV risk calculator, which uses data on patient's gender, age, and clinical characteristics to calculate risk. Baseline characteristics, primarily derived from Younossi et al. 2019,[2] on gender, age, total cholesterol, high-density lipoprotein (HDL), and diabetes status, were used as input values in the calculation and 10-year CV risk in each arm of the model was estimated
- In the scenario analysis, it was assumed that active treatments would have identical fibrosis outcomes as estimated in the placebo arm, with changes in lipid levels, including HDL, low-density lipoprotein (LDL), and triglycerides (TG), being the only parameters explored to assess impact on overall cost-effectiveness. Based on published evidence, change in lipid levels versus placebo was estimated for resmetirom (HDL: +3.80%; LDL: -17.30%; TG: -36.00%)[3] and OCA (HDL: -8.67%; LDL: +15.07%; TG: -21.64%)[2]
- Monte Carlo simulation was used to demonstrate the parameter uncertainty by sampling lipid parameters and other parameters that impact CV event costs and quality-adjusted life years (QALYs), such as MI and stroke probabilities, from their respective distributions. Probabilities of four CV events were explored, including MI alone, stroke alone, MI after stroke, and stroke after MI

## RESULTS

- Results of the scenario analysis showed the impact of treatment strategies on increasing or decreasing lipid levels, i.e., variations led to changes in costs and quality-of-life due to changes in the probability of occurrence of MI and stroke
- Overall, the lifetime CVD event risk including associated mortality for resmetirom, OCA, and placebo was 46.67%, 61.97%, and 60.28%, respectively
- **Table 1** presents the breakdown occurrence of each nonfatal CV event over the lifetime horizon for each treatment strategy

**Table 1. Lifetime nonfatal CV events breakdown per treatment strategy (% (SD))**

| | Resmetirom | Placebo | OCA |
|---|---|---|---|
| **MI alone** | 26.59% (3.91) | 33.75% (4.95) | 34.65% (5.11) |
| **Stroke alone** | 6.09% (2.44) | 7.42% (2.99) | 7.58% (3.06) |
| **MI after stroke** | 2.02% (0.63) | 3.26% (0.97) | 3.44% (1.02) |
| **Stroke after MI** | 1.74% (0.59) | 2.73% (0.91) | 2.86% (0.96) |

- Annual occurrence of nonfatal CV events is shown in **Figure 1**
- Lifetime CVD-associated mortality rates were estimated at 10.91%, 14.48%, and 14.09% for resmetirom, OCA, and placebo, respectively
- **Figure 2** compares overall survival and CV event free across treatment strategies
- Over a lifetime horizon, changes in CVD events led to a QALY gain of 0.152 for resmetirom and a QALY loss of 0.135 for OCA compared with placebo
- Per patient costs of CVD events were decreased by $5,785 with resmetirom and increased by $719 with OCA. Net monetary benefits of $21,029 and -$14,264 for CVD events were estimated for resmetirom and OCA, respectively

## LIMITATIONS

- This analysis explored the impact of various potential treatments for NASH on lipid levels. Other competing risks, such as changes in lifestyle or effect of other treatments (eg, statins) were excluded. We assumed that only treatment-related changes in lipid levels would impact CV events

**Figure 1. Annual nonfatal CV event rates breakdown over the lifetime horizon**

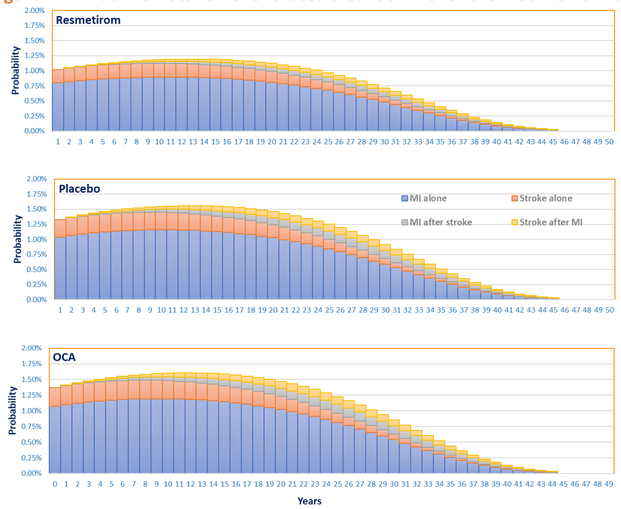
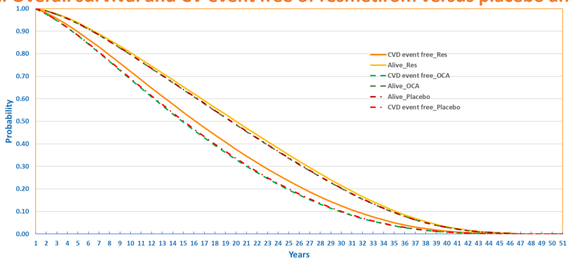



**Figure 2. Overall survival and CV event free of resmetirom versus placebo and OCA**




## CONCLUSIONS

- **Changes in CV event risk factors are strong drivers of cost-effectiveness in economic evaluations of treatments for NASH**
- **NASH therapies that reduce lipid levels may enhance the effect of fibrosis improvement, leading to improved quality-of-life and reduced costs**

## REFERENCES

1. Javanbakht M, et al. *Pharmacoecon Open*. 2023;7(1):93-110.
2. Younossi ZM, et al. *Lancet*. 2019;394(10215):2184-2196.
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