Metabolomic and Lipidomic Analysis of Patients With Presumed Metabolic Dysfunction-Associated Steatohepatitis (MASH) Treated With the Selective Glucocorticoid Receptor Modulator Miricorilant

PRESENTER:
Kris V. Kowdley, MD
Contact: kkowdley@liverinstitutenw.org

Kris V. Kowdley,[1] Mazen Noureddin,[2] Elizabeth Parks,[3] Jeffrey Botbyl,[4] Rafael Mayoral Monibas,[4] Subhagya Wadekar,[4] Aprille Espinueva,[4] Kavita Juneja,[4] Andrew Schwab,[5] Naim Alkhouri[6]

[1]Liver Institute Northwest, Seattle, WA; [2]Houston Research Institute, Houston, TX; [3]University of Missouri School of Medicine, Columbia, MO; [4]Corcept Therapeutics Incorporated, Menlo Park, CA; [5]Metabolon, Durham, NC; [6]Arizona Liver Health, Tucson, AZ

Summary & Conclusions

- The observed declines in intermediate lipid species suggest that responders (patients with ≥30% reduction from baseline in LFC following miricorilant treatment), particularly those with rapid LFC clearance accompanied by efficacy-associated ALT elevations (rapid responders [RR]), experienced enhanced metabolic clearance of lipids and FAs
  - In RRs, metabolic clearance of acylglycerols continued to improve at week 12 despite discontinuation or interruption of miricorilant after week 6
- Rapid changes in liver metabolism, such as increased FA oxidation, can cause transient hepatic stress. This stress may produce a short-term rise in ALT levels as the liver adjusts to the new metabolic conditions
  - Although this may cause transient hepatic stress, it points to improved hepatic lipid metabolism
- Changes in bile metabolism could suggest elevated liver capacity to synthesize bile acids, enhancing lipid emulsification or clearance
- The ongoing phase 2b MONARCH study is assessing 100 mg miricorilant twice weekly, a dose that resulted in improved LFC without ALT elevations in miricorilant's phase 1b study, and a higher dose of 200 mg twice weekly after a 6-week lead-in of 100 mg twice weekly

ALT, alanine aminotransferase; FA, fatty acid; LFC, liver fat content.

The authors want to thank all those who participated in this study: The study patients and their families, the investigators, and the sponsor team.

Scan QR code to download poster

Poster number: 3205

Background

- Cortisol activity has been implicated in metabolic dysfunction-associated steatotic liver disease (MASLD) development and progression[1,2]
  - Cortisol binding to the glucocorticoid receptor (GR) increases availability of energy substrates, such as free fatty acids (FFAs), for daytime activities and stress response
  - Cortisol can contribute to increased lipid levels in the liver by increasing uptake and de novo lipogenesis
- Miricorilant (**Figure 1**) is an orally delivered, nonsteroidal selective glucocorticoid receptor modulator (SGRM) that acts as a mixed GR agonist/antagonist and modest mineralocorticoid receptor (MR) antagonist (6-fold higher affinity for GR vs MR) and may reduce hepatic steatosis by modulating cortisol activity in the liver[3]
- In MASLD/MASH preclinical models, miricorilant reversed and prevented hepatic steatosis by preventing lipid accumulation in the liver and reduced inflammation, fibrosis stage, and NAS[4]
- In a phase 1b, multicohort, open-label, dose-finding study (NCT05117489), adults with presumed MASH with fibrosis treated with 30—200 mg miricorilant dosed daily or intermittently for 12 or 24 weeks had notable and rapid liver fat content (LFC) decreases, which was occasionally accompanied by efficacy-associated alanine aminotransferase (ALT) increases[5]
  - Miricorilant 100 mg twice weekly was safe, well-tolerated, and resulted in reduced LFC (-28.2% at week 12), with a corresponding decline in liver enzymes and improved hepatic, lipid, and glycemic markers[5]
  - Miricorilant 100 mg twice weekly is being assessed in the phase 2b MONARCH study (NCT06108219)

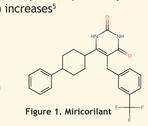


Figure 1. Miricorilant

Aim

- This metabolomic analysis of the phase 1b study data explored miricorilant's mechanism of reducing LFC with the following aims:
  - Test the hypothesis that rapid enhancement in metabolic activity can lead to transient ALT elevations
  - Characterize metabolomic profiles in plasma from responders vs nonresponders following miricorilant treatment
  - Assess biochemical differences in responders with and without efficacy-associated ALT elevations

Methods

- Plasma samples taken at baseline and weeks 6 and 12 from select patients in the first 10 study cohorts were stratified into 3 groups based on response regardless of miricorilant dose received:
  - **Standard responders (SRs):** ≥30% reduction from baseline in LFC without ALT elevations (n=11)
  - **Rapid responders (RRs):** ≥30% reduction from baseline in LFC with treatment efficacy-associated ALT elevations >3× upper limit of normal (n=9)
  - **Nonresponders (NRs):** without reduction from baseline in LFC (n=11)
- Lipidomic profiles in serum were assessed via liquid chromatography/mass spectrometry
- Metabolite changes within each responder group over time (baseline to week 6, baseline to week 12, week 6 to 12) and between groups at specified time points were analyzed using fold change correlations
- Results were analyzed by 2-way repeated-measures analysis of variance and matched pairs t-test

NAS, nonalcoholic fatty liver disease activity score.

1 Results: Demographic Characteristics

- NRs were selected to match RRs and SRs based on demographic characteristics (race, sex, and age; **Table 1**)

Table 1. Baseline Patient Characteristics

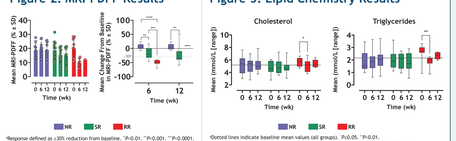
	SRs (n=11)	RRs (n=9)	NRs (n=11)
Age group, n (%)			
<30 y	0	0	2 (18.2)
30 to 50 y	4 (36.4)	4 (44.4)	3 (27.3)
>50 y	7 (63.6)	5 (55.6)	6 (54.5)
Female, n (%)	7 (63.6)	5 (55.6)	6 (54.5)
Race, n (%)			
White	11 (100)	8 (88.9)	11 (100)
Asian	0	1 (11.1)	0
Hispanic or Latino ethnicity, n (%)	7 (63.6)	5 (55.6)	6 (54.5)
BMI, n (%)			
30 to <35 kg/m²	2 (18.2)	5 (55.6)	4 (36.4)
35 to <40 kg/m²	4 (36.4)	1 (11.1)	4 (36.4)
≥40 kg/m²	4 (36.4)	2 (22.2)	2 (18.2)
Liver stiffness, n (%)		*(n=8)*	
8.5 to 12 kPa	6 (54.5)	4 (50.0)	10 (90.9)
>12 kPa	5 (45.4)	4 (50.0)	1 (9.1)
MRI-PDFF %, mean (SD)	18.7 (6.7)	20.3 (6.7)	17.9 (5.6)
Hypertension, n (%)	5 (45.4)	5 (55.6)	7 (63.6)
Diabetes, n (%)	7 (63.6)	2 (22.2)	3 (27.3)

BMI, body mass index; MRI-PDFF, magnetic resonance imaging derived proton density fat fraction; NR, nonresponder; RR, rapid responder; SD, standard deviation; SR, standard responder.

2 Results: Liver Fat Content and Lipid Chemistry

- In the initial 6-week treatment period, RRs lost liver fat ~2.9× faster (-50.4%) than SRs (-17.5%) **(Figure 2)**
  - Of the 9 RRs, study drug was discontinued in 8 and interrupted in 1 after week 6 due to ALT elevation
- The RR group also showed significant decreases in plasma cholesterol and triglycerides from baseline to week 6 **(Figure 3)**
  - There were no statistically significant changes in high- or low-density lipoprotein

Figure 2. MRI-PDFF Results



[a]Response defined as ≥30% reduction from baseline. *P<0.01. **P<0.001. ***P<0.0001. MRI-PDFF, magnetic resonance imaging proton density fat fraction; NR, nonresponder; RR, rapid responder; SD, standard deviation; SR, standard responder.

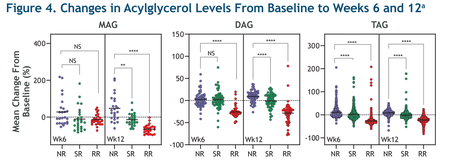
Figure 3. Lipid Chemistry Results[a]

[a]Dotted lines indicate baseline mean values (all groups). †P≤0.05. ‡P<0.01. NR, nonresponder; RR, rapid responder; SD, standard deviation; SR, standard responder.

3 Results: Acylglycerols

- At week 6, both responder groups showed notably lower acylglycerol levels (SR: +2.6%; RR: -26.8%) vs NRs (+10.8%), with significant between-group differences for triacylglycerols **(Figure 4)**
  - Reductions in acylglycerols most associated with inflammation (monoacylglycerols and diacylglycerols) were more prominent in RRs **(Table 2)**
  - Acylglycerol level decreases continued at week 12 in RRs despite drug discontinuation for 8 of 9 patients after week 6, suggesting enhanced metabolic regulation persisted in this group after drug exposure ended

Figure 4. Changes in Acylglycerol Levels From Baseline to Weeks 6 and 12[a]



[a]1-way analysis of variance multiple comparisons Dunnett post-test. *P<0.01. **P<0.0001. DAG, diacylglycerol; MAG, monoacylglycerol; NR, nonresponder; NS, not significant; RR, rapid responder; SR, standard responder; TAG, triacylglycerol.

Table 2. Fold Changes in Acylglycerol Levels From Baseline to Week 6 and Week 12[a]

Categories Biochemical Name/Ratio	NR Wk6/BL	NR Wk12/BL	SR Wk6/BL	SR Wk12/BL	RR Wk6/BL	RR Wk12/BL
DAG (16:0/16:0)	1.10	1.14	0.71	0.84	0.88	0.51
DAG (16:0/18:0)	1.03	1.03	0.40	0.85	0.74	0.33[†]
DAG (16:0/22:5)	1.07	1.25	0.98	0.96	0.73[†]	0.49[†]
TAG 52:5-FA14:0	1.07	1.13	0.96	0.91	0.70[†]	0.66[†]
TAG 52:5-FA22:5	1.13	1.18	0.94	0.93	0.64[†]	0.59[†]
TAG 52:6-FA14:0	1.23	1.32	0.97	0.97	0.59[†]	0.51[†]
TAG 56:7-FA22:5	1.21	1.32	0.93	0.97	0.66[†]	0.46[†]
TAG 56:7-FA22:4	1.03	1.14	0.85	0.99	0.65[†]	0.59[†]
MAG (17:0)	1.27	2.46	0.47	0.47	0.85	0.86
MAG (22:6)	3.12	2.00	0.56	0.72	0.61	0.39[†]

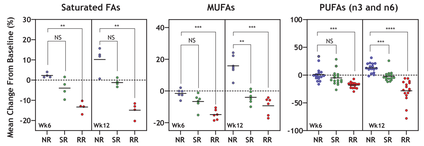
Decreased Trajectory (Fold change <1) Increased Trajectory (Fold change >1)

[a]Color scheme based on a 3-color scale with minimum of 0.22, midpoint 1, and maximum 2. †P≤0.05. ‡0.05<P<0.10. BL, baseline; DAG, diacylglycerol; FA, fatty acid; MAG, monoglyceride; NR, nonresponder; RR, rapid responder; SR, standard responder; TAG, triacylglycerol.

4 Results: Long-chain Fatty Acids

- Most long-chain FAs (LCFAs), including polyunsaturated FAs (PUFAs) omega-3 and -6, were reduced (fold change <1) at week 6 and week 12 vs baseline in responders regardless of ALT elevation but were elevated (fold change >1) in NRs **(Table 3 and Figure 5)**
  - Significant reductions were observed at week 6 for SRs (-5.3%; *P*<0.01) and RRs (-16.6%; *P*<0.0001) but not NRs (+0.6%) vs their respective baselines
  - Decreases in LCFAs and PUFAs may suggest improved FA oxidation in responders, which would be expected to reduce circulating FFAs

Figure 5. Changes in LCFA Levels From Baseline to Weeks 6 and 12[a]



[a]1-way analysis of variance multiple comparisons Dunnett post-test. *P<0.01. **P<0.001. ***P<0.0001. FA, fatty acid; LCFA, long-chain FA; MUFA, monounsaturated FA; NR, nonresponder; NS, not significant; PUFA, polyunsaturated FA; RR, rapid responder; SR, standard responder.

Table 3. Fold Changes in LCFA Levels From Baseline to Weeks 6 and 12[a]

LCFAs	Categories Biochemical Name/Ratio	NR Wk6/BL	NR Wk12/BL	SR Wk6/BL	SR Wk12/BL	RR Wk6/BL	RR Wk12/BL
Saturated FAs	Myristate (14:0)	1.02	1.16	1.02	0.98	0.87	0.88
	Pentadecanoate (15:0)	1.01	1.13	0.94	0.99	0.87	0.87
	Margarate (17:0)	1.02	1.12	0.90	0.97	0.83	0.80
MUFAs	Myristoleate (14:1n5)	1.00	1.16	0.95	0.93	0.82	0.94
	Palmitoleate (16:1n7)	0.94	1.22	0.94	0.97	0.85	0.96
	10-heptadecenoate (17:1n7)	0.98	1.24	0.85	0.90	0.81	0.85
	Oleate/vaccenate (18:1)	1.00	1.13	0.99	1.01	0.89	0.92
	10-nonadecenoate (19:1n9)	0.97	1.05	0.92	0.95	0.85	0.83
	Eicosenoate (20:1)	1.02	1.15	0.96	1.00	0.88	0.94
PUFAs (n-3 and n-6)	Tetradecadienoate (14:2)	0.99	1.04	1.03	1.04	0.82	0.73
	Stearidonate (18:4n3)	1.34	1.21	1.16	0.94	0.77	0.63
	Eicosapentaenoate (EPA; 20:5n3)	0.98	1.20	1.01	1.03	0.70	0.22
	Docosapentaenoate (n3 DPA; 22:5n3)	0.89	1.10	0.90	0.95	0.77	0.36
	Docosahexaenoate (DHA; 22:6n3)	0.89	0.98	0.85	0.88	0.77	0.68
	Docosatrienoate (22:3n3)	0.95	1.22	0.73	0.91	0.85	0.67
	Hexadecadienoate (16:2n6)	1.03	1.15	0.98	1.00	0.83	0.87
	Linoleate (18:2n6)	1.08	1.20	0.96	1.01	0.85	0.94
	Linolenate [alpha or gamma; (18:3n3 or 6)]	1.26	1.31	0.99	0.96	0.81	0.94
	Dihomo-linoleate (20:2n6)	1.01	1.13	0.90	0.97	0.85	0.83
	Arachidonate (20:4n6)	0.97	1.10	0.86	0.95	0.84	0.72
	Adrenate (22:4n6)	0.84	1.11	0.83	0.89	0.84	0.75
	Docosapentaenoate (n6 DPA; 22:5n6)	0.94	1.00	0.91	0.95	0.86	0.86
	Docosadienoate (22:2n6)	0.99	1.02	0.91	1.00	0.93	0.89
	Mead acid (20:3n9)	1.05	1.12	1.28	1.26	0.76	0.59[†]

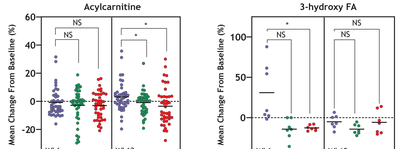
Decreased Trajectory (Fold change <1) Increased Trajectory (Fold change >1)

[a]Color scheme based on a 3-color scale with minimum of 0.22, midpoint 1, and maximum 1.34. †0.05<P<0.10. BL, baseline; FA, fatty acid; LCFA, long-chain FA; MUFA, monounsaturated FA; NR, nonresponder; PUFA, polyunsaturated FA; RR, rapid responder; SR, standard responder.

5 Results: Fatty Acid ß-Oxidation

- Many short- to medium-chain acylcarnitine species were reduced (fold change <1) in RRs vs increased in NRs (fold change >1) (**Table 4**)
  - Lower levels can reflect improved utilization by the mitochondria at the tissue level
- 3-hydroxy FA species were significantly reduced for RRs at week 6 vs NRs (*P*≤0.05), pointing to improved liver FA oxidation (**Figure 6**)

Figure 6. Changes in Acylcarnitine and 3-hydroxy FA Levels From Baseline to Weeks 6 and 12[a]



[a]1-way analysis of variance multiple comparisons Dunnett post-test. †P≤0.05. FA, fatty acid; NR, nonresponder; NS, not significant; RR, rapid responder; SR, standard responder.

Table 4. Fold Changes in Acylcarnitine and 3-hydroxy FA Levels From Baseline to Weeks 6 and 12[a]

Acylcarnitine/ 3-hydroxy FA	Categories Biochemical Name/Ratio	NR Wk6/BL	NR Wk12/BL	SR Wk6/BL	SR Wk12/BL	RR Wk6/BL	RR Wk12/BL
Short Chain	Acetylcarnitine (C2)	0.90[†]	0.98	1.00	0.93	0.92	0.99
Medium Chain	Hexanoylcarnitine (C6)	0.90	1.03	1.00	0.95	0.87	0.99
	Octanoylcarnitine (C8)	1.03	1.09	1.01	1.01	0.81	0.84
	Nonanoylcarnitine (C9)	0.96	0.96	1.03	1.01	0.82	0.79[†]
	Laurylcarnitine (C12)	1.00	1.05	1.11	1.03	1.00	0.87
Long Chain Saturated	Myristoylcarnitine (C14)	0.93	0.99	1.05	1.02	1.01	0.91
	Palmitoylcarnitine (C16)	0.94	0.99	1.07	1.02	0.97	0.88
	Margaroylcarnitine (C17)	0.90	0.99	0.98	0.93	0.92	0.89
	Stearoylcarnitine (C18)	0.93	0.89	1.00	0.94	0.97	0.86[†]
	Arachidoylcarnitine (C20)	1.00	1.00	1.00	1.01	0.89	0.90
	Behenoylcarnitine (C22)	1.09	0.96	0.85	0.87	1.09	0.90
	Lignoceroylcarnitine (C24)	0.96	0.93	0.88	1.00	1.07	1.03
	Cerotoylcarnitine (C26)	1.01	1.05	1.07	1.03	1.06	1.04
3-hydroxy Metabolism	3-hydroxyhexanoate	1.04	0.92	0.86	0.91	0.91	0.93
	3-hydroxyoctanoate	1.61	1.07	0.78	0.78	0.83	1.14
	3-hydroxydecanoate	1.54	1.01	0.88	0.81	0.84	0.97
	3-hydroxysebacate	1.88	1.00	0.64	0.82	0.92	1.12
	3-hydroxylaurate	1.09	0.93	1.00	0.90	0.86	0.80
	3-hydroxymyristate	0.98	0.89	1.00	0.95	0.88	0.81
	3-hydroxystearate	1.02	0.82	0.84	0.84	0.86	0.83
	3-hydroxyoleate	0.75[†]	0.83	0.82	1.20	1.12	0.73[†]

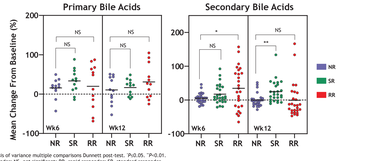
Decreased Trajectory (Fold change <1) Increased Trajectory (Fold change >1)

[a]Color scheme based on a 3-color scale with minimum of 0.22, midpoint 1, and maximum 1.34. †P≤0.05. ‡0.05<P<0.10. BL, baseline; FA, fatty acid; NR, nonresponder; RR, rapid responder; SR, standard responder.

6 Results: Bile Acids

- At baseline, ~70% of the analyzed primary and secondary bile acids showed elevated levels in RRs compared with SRs and NRs
- For the SR and RR within-group comparisons, most primary bile acid species did not change significantly from baseline to weeks 6 or 12 **(Table 5 and Figure 7)**
  - For RRs, numerous secondary bile acid species were significantly shifted bidirectionally from baseline
- At week 6, RRs had increasing trajectories (several significant) vs NRs for numerous primary and secondary bile acid species
  - SRs trended toward increased bile acid species vs NRs
  - In SRs, most primary bile acids decreased by ~19% from week 6 to week 12

Figure 7. Changes in Bile Acid Levels From Baseline to Weeks 6 and 12[a]



[a]1-way analysis of variance multiple comparisons Dunnett post-test. †P≤0.05. *P<0.01. NR, nonresponder; NS, not significant; RR, rapid responder; SR, standard responder.

Table 5. Fold Changes in Bile Acid Levels From Baseline to Weeks 6 and 12[a]

Bile Acid	Categories Biochemical Name/Ratio	NR Wk6/BL	NR Wk12/BL	SR Wk6/BL	SR Wk12/BL	RR Wk6/BL	RR Wk12/BL	Wk 6 SR/NR	Wk 6 RR/NR	RR/SR
Primary	Cholate	0.57	0.47	1.14	1.49	0.39	1.93	2.19	2.63	1.20
	Glycocholate	1.34	1.51	1.11	0.88	1.55	1.36	2.55	4.00	1.57
	Taurocholate	1.24	1.44	1.39	1.05	1.83	0.75	1.95	4.21	2.16
	Chenodeoxycholic acid sulfate	1.09	0.96	1.66	1.39	0.68	1.27	1.10	0.86	0.78
	Glycochenodeoxycholate	1.22	1.43	1.25	1.23	0.96	0.93	2.42	2.77	1.15
	Taurochenodeoxycholate	1.16	1.35	1.59	1.28	1.12	0.95	2.38	3.35	1.40
	Cholic acid glucuronide	1.50	0.70	1.51	0.98	0.86	1.82	1.10	1.25	1.13
	Glycochenodeoxycholate glucuronide	1.18	0.92	0.92	0.92	1.49	0.85	1.23	1.81[†]	1.48
	Glycochenodeoxycholate 3-sulfate	1.21	1.49	0.86	0.93	1.87	1.44	1.62	4.80	2.97
Secondary	Deoxycholate	1.10	0.84	0.97	1.13	0.59	0.87	0.99	1.21	1.21
	Deoxycholic acid glucuronide	1.06	0.88	1.30	0.96	0.82	1.26	1.31	1.52	1.16
	Glycodeoxycholate	1.06	0.87	1.43	1.52[†]	1.05	0.84	1.34	2.25	1.67
	Taurodeoxycholate	1.00	0.81	1.73	1.55[†]	0.99	0.84	0.97	1.69	1.75[†]
	Taurodeoxycholic acid 3-sulfate	0.81	0.71	1.34	1.24	1.78	0.63	1.61	2.65	1.64
	Lithocholic acid sulfate	1.36	1.23	0.93	1.46	1.94	2.67	1.04	4.06	3.90
	Glycolithocholate sulfate	1.06	0.93	0.79	0.93	1.89	1.04	1.22	2.25[†]	1.84[†]
	Ursodeoxycholate	0.84	0.86	1.62	2.34	0.32	0.62[†]	1.26	0.75	0.60
	Glycoursodeoxycholate	1.46	1.45	1.40	1.16	0.61	0.56	2.30	1.72	0.75
	Glycoursodeoxycholic acid sulfate	1.04	0.99	0.95	1.07	1.35	0.58	1.50	3.80	2.54
	Tauroursodeoxycholate	0.92	1.00	1.92	1.16	0.66	0.53	3.59	3.04	0.85
	Tauroursodeoxycholic acid sulfate	1.06	0.98	1.10	1.10	2.07	0.61	1.58	5.65	4.20
	Hyocholate (gamma-muricholate)	1.10	0.98	1.13	0.97	1.11	1.45	0.89	1.50	1.69
	Glycocholenate sulfate	0.97	1.03	0.94	0.92	1.43[†]	0.88	1.14	2.09	1.84
	Taurocholenate sulfate	0.84	0.99	1.06	1.08	1.55[†]	0.69	1.26	2.15	1.70
	3beta-hydroxy-5-cholenoate	0.96	1.05	1.07	1.07	1.24	0.87	0.73	1.03	1.41[†]
	Glycodeoxycholate 3-sulfate	0.98	0.88	1.01	1.25	1.79[†]	0.77	1.47	3.39[†]	2.30
	Taurochenodeoxycholic acid 3-sulfate	1.19	1.38	1.09	1.23	2.43[†]	1.21	1.65	5.48[†]	3.31[†]

Decreased Trajectory (Fold change <1) Increased Trajectory (Fold change >1)

[a]Color scheme based on a 3-color scale with minimum of 0.35, midpoint 1, and maximum 6.65. †P≤0.05. ‡0.05<P<0.10. NR, nonresponder; RR, rapid responder; SR, standard responder.

References

(1) Rahimi L, et al. *Diabetes Metab Syndr Obes.* 2020;13:1133-1145.
(2) Rinella ML, et al. *Hepatology.* 2023;77(5):1797-1835.
(3) Hunt HJ, et al. *Bioorg Med Chem Lett.* 2012;22(24):7376-7380.
(4) Koorneef LL, et al. *Endocrinology.* 2018;159(12):3925-3936.
(5) Alkhouri N, et al. Presented at: NASH-TAG 2024; January 4-6, 2024; Park City, UT.

Acknowledgements

This study is sponsored by Corcept Therapeutics, Inc. Medical writing assistance was provided by Valerie Hilliard, PhD, of Corcept Therapeutics, Inc and R&R Healthcare Communications.

The authors would like to posthumously acknowledge Stephen A. Harrison for his contributions to this study.

Presenter Disclosures

Dr. Kowdley: research support from 89bio, CymaBay, Ipsen, Genfit, Gilead, GSK, Hanmi, HighTide, Intercept, Madrigal, Mirum, NGM, Pfizer, Pliant, and Viking; royalties/licenses from UpToDate; consulting fees from 89bio, Calliditas Therapeutics, CymaBay Therapeutics, Genfit, Gilead, Irigiharm, Intercept, Madrigal, Mirum, NGM, and Pliant; payment/honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from AbbVie, Gilead, and Intercept.