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# VANOGLIPEL (DA-1241), A GPR119 AGONIST, DEMONSTRATES HEPATOPROTECTIVE EFFECTS THROUGH IMPROVING INFLAMMATION AND METABOLISM IN THE LIVER: A 16-WEEK RANDOMIZED PLACEBO-CONTROLLED TRIAL IN PRESUMED MASH PATIENTS

#4012


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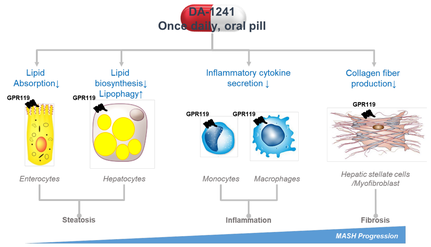
MetaVia DONG-A ST

## INTRODUCTION

- ☑ Vanoglipel (DA-1241), a potent and selective agonist for G protein-coupled receptor 119 (GPR119)
- ☑ Vanoglipel increased the secretion of insulin and glucagon-like peptide-1 (GLP-1) and demonstrated post-prandial glucose-lowering efficacy in type 2 diabetic patients (NCT03646721).
- ☑ Vanoglipel alleviates liver steatosis by suppressing de novo lipogenesis and enhancing lipolysis, decreases liver inflammation by suppressing macrophage activation and differentiation, and mitigates liver fibrosis by inhibiting the activation of hepatic stellate cells.

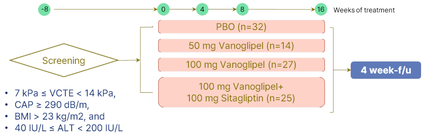



## AIM

This phase 2a trial evaluated the efficacy and safety of vanoglipel as a potential treatment for MASH, alone and in combination with a dipeptidyl peptidase 4 inhibitor (DPP4i) to augment endogenous GLP-1 action.

## METHOD

Total 109 subjects with presumed MASH and qualifying baseline alanine transaminase (ALT) and imaging analysis were randomized to receive placebo (PBO), vanoglipel 50 mg, vanoglipel 100 mg alone, or vanoglipel 100 mg with a DPP4 inhibitor (Combo) in a 2:1:2:2 ratio once daily for 16 weeks (NCT06054815).



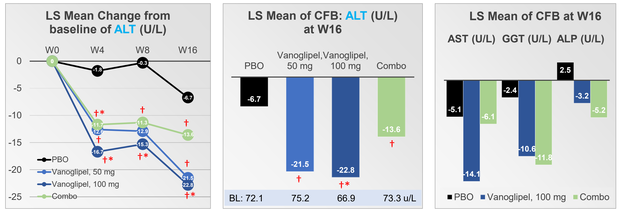

## RESULTS

### Baseline Characteristics of the ITT Population

| Mean (SD) | PBO | Vanoglipel 50 mg | Vanoglipel 100 mg | Vanoglipel 100 mg /DPP4i Combo | All subjects |
|---|---|---|---|---|---|
| N | 32 | 14 | 27 | 36 | 109 |
| Age, years | 51.31 (12.92) | 53.29 (11.78) | 54.04 (13.04) | 48.36 (12.64) | 51.27 (12.75) |
| Female, n (%) | 16 ( 50.0) | 8 ( 57.1) | 14 ( 51.9) | 20 ( 55.6) | 58 ( 53.2) |
| VCTE (kPa) | 10.16 (2.24) | 10.56 (2.02) | 10.15 (2.16) | 9.99 (2.19) | 10.15 (2.15) |
| CAP (dB/m) | 343.66 (31.78) | 344.21 (32.99) | 336.65 (32.63) | 346.39 (33.58) | 342.95 (32.50) |
| FAST Score | 0.546 (0.168) | 0.592 (0.170) | 0.536 (0.169) | 0.571 (0.165) | 0.558 (0.166) |
| BMI (kg/m$^2$) | 37.73 (7.01) | 39.56 (7.09) | 38.29 (5.72) | 37.94 (7.22) | 38.17 (6.73) |
| Type 2 Diabetes n, (%) | 13 (40.6) | 6 (42.9) | 16 (59.3) | 15 (41.7) | 50 (45.9) |

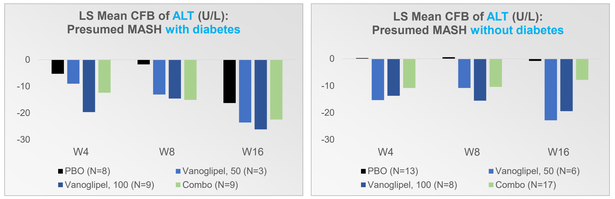
### Vanoglipel Decreased Plasma Liver Enzymes after 16-Week Treatment

- After 16 weeks of treatment, there were slight but significant body weight changes only in PBO and vanoglipel 50 mg-treated groups (data not shown)
- In subgroup with 40 ≤ ALT< 200 U/L at baseline, vanoglipel significantly decreased plasma ALT
- Decrease in ALT was NOT augmented by enhanced endogenous incretin action in the combo group, suggesting dominant efficacy of vanoglipel monotherapy



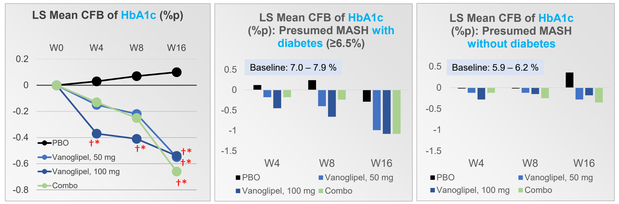

†, 95% CI does not cross 0; *, p<0.05 vs. PBO; PBO (N=21), Vanoglipel 50 mg (N=9), Vanoglipel 100 mg (N=17), Combo (N=26)
BL: baseline

- Vanoglipel significantly decreased plasma ALT regardless of glucose control




### Vanoglipel Improved Glucose Control in Presumed MASH Patients

- Vanoglipel decreased the levels of glycated hemoglobin from the 4th week of treatment
- Enhanced incretin action (-0.66%p) augmented glucose control compared to vanoglipel monotherapy (-0.54%p) at Week 16
- Vanoglipel efficiently controlled plasma glucose in prediabetic and diabetic subjects diagnosed presumed MASH

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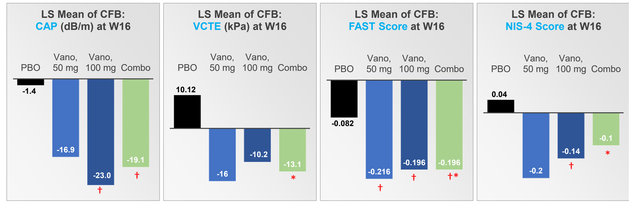
### Vanoglipel Improved Liver Steatosis and Fibrosis in at-risk MASH

- Vanoglipel improved liver steatosis (CAP) and liver fibrosis (VCTE)
- Vanoglipel alleviated non-invasive FAST and NIS-4 score for at-risk MASH from baseline
- Decrease in ALT was NOT augmented by enhanced endogenous incretin action in the combo group, suggesting the limitation of endogenous GLP-1 effect



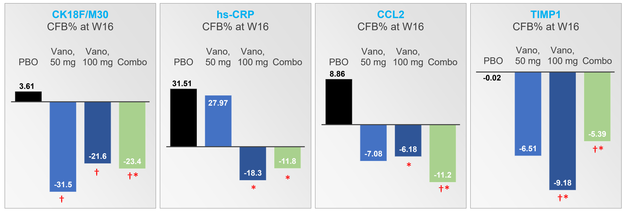

†, 95% CI does not cross 0; *, p<0.05 vs. PBO; PBO (N=21), Vanoglipel 50 mg (N=9), Vanoglipel 100 mg (N=17), Combo (N=26). For exploratory analysis, N may differ as it is based on observed data only. Abbreviation: CAP, controlled attenuation parameter; VCTE, vibration-controlled transient elastography; FAST, FibroScan-AST; NIT-4, non-invasive blood-based algorithm for MASH Identification and Stratification, calculated using 4 independent biomarkers

## CONCLUSIONS

- ☑ Vanoglipel treatment was well tolerated in presumed MASH patients, with no TEAE leading to treatment discontinuation in any treatment groups except one in the PBO group
- ☑ Vanoglipel treatment reduced serum ALT and CAP score at week 16
- ☑ Significant reduction in VCTE was observed in the combination treatment
- ☑ Hepatoprotective effects correlated with improvement in NITs and are likely attributed to its anti-inflammatory and antifibrosis effects
- ☑ Vanoglipel reduced disease-associated lipids in plasma lipidomic profiles
- ☑ Vanoglipel efficiently improved glucose control in patients with comorbidity of prediabetes and type 2 diabetes

### Vanoglipel Treatment Improved Inflammation and Fibrosis Status

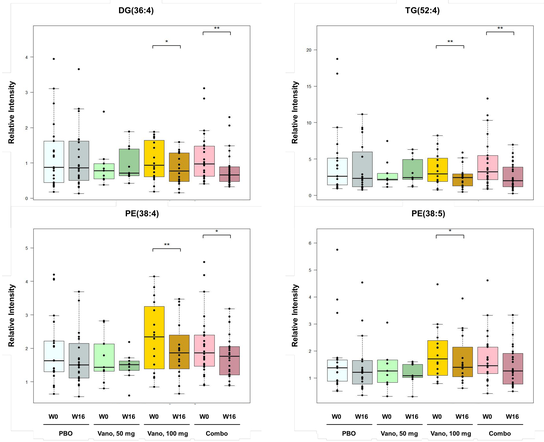
- Vanoglipel reduced circulating biomarkers of cell death (CK18F/M30), inflammation (hs-CRP, CCL2), and fibrosis (TIMP1)




†, 95% CI does not cross 0; *, p<0.05 vs. PBO; PBO (N=21), Vanoglipel 50 mg (N=9), Vanoglipel 100 mg (N=17), Combo (N=26)

### Vanoglipel Reduced Pathogenic Lipids in Plasma Lipidomic Profiles

- Vanoglipel 100 mg reduced plasma glycerolipids (DG36:4, TG52:4) and glycerophospholipids (PE38:4, PE38:5)




*, p<0.05 vs. W1 in each group; PBO (N=21), Vanoglipel 50 mg (N=9), Vanoglipel 100 mg (N=17), Combo (N=26)

## REFERENCES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