CASE STUDIES FROM COVALENT-111, A PHASE 1/2 TRIAL OF BMF-219, A COVALENT MENIN INHIBITOR, IN PATIENTS WITH TYPE 2 DIABETES

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Background

- T2D is characterized by hyperglycemia due to a gradual decline in beta-cell function
- Menin, a scaffold protein, is as an important regulator of glycemic control, whereby inhibition of menin enhances beta cell proliferation and function
- BMF-219 is an oral covalent menin inhibitor in clinical development for the management of T2D and T1D
- In preclinical diabetes ZDF and STZ rat models, BMF-219 showed durable glycemic control following short-term treatment [1,2]
- In a multiple ascending dose (MAD) cohorts in patients with T2D, 4 weeks of BMF-219 100 and 200mg once daily dosing improved glycemic control at Week 26 and was generally safe and well tolerated[3]
- Here, we highlight two BMF-219-treated T2D patients who demonstrated significant efficacy in a double blind randomized-controlled trial

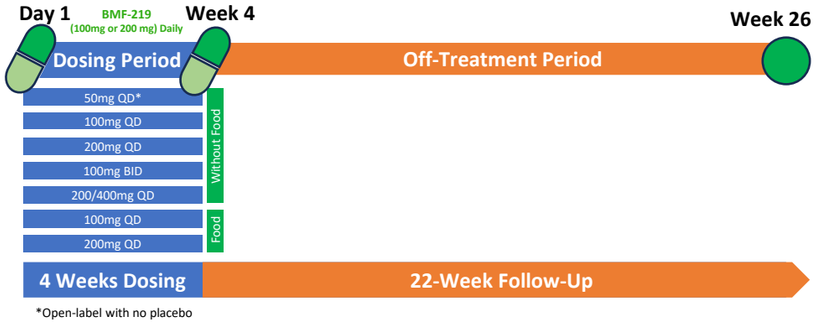
Aim

- To assess the safety and efficacy of BMF-219 once daily treatment for 4 weeks at Week 26 (22 weeks after final dose)

Methods

- In COVALENT-111, adults with T2D receiving up to 3 antidiabetic agents received BMF-219 with or without food once daily for 4 weeks in MAD cohorts (50, 100, 200, and 400mg), with follow-up until Week 26
- Key eligibility criteria: Adults with T2D treated with up to 3 antidiabetic agents (excluding insulin secretagogues and insulin), HbA1c 7%-10.5%, diabetes duration ≤15 years
- Primary endpoint: Safety and tolerability
- Secondary endpoints: Measures of glycemic control (HbA1c, CGM), beta cell function (HOMA-B and C-peptide), and durability of glycemic response

Study Design



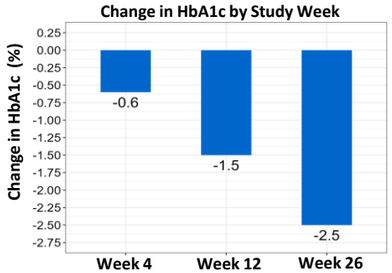
*Open-label with no placebo

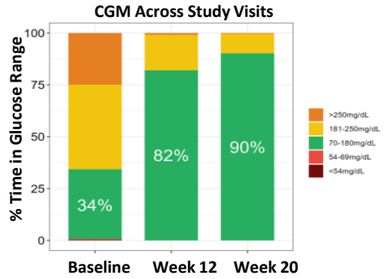
Results

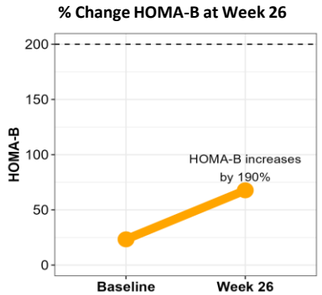
Case Study 1

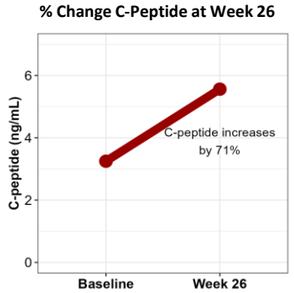
- 29-year-old man with 4-year history of T2D
- Metformin 500 mg BID, empagliflozin 25 mg BID
- HbA_{1c} 9.5%; FPG 134 mg/dL; BMI 25.6 kg/m^2
- CGM TIR 34%

- BMF-219 200 mg QD without food for 4 weeks
- Metformin and SGLT2i continued
- No adverse events reported
- At (Week 26), HbA1c 7.0% (change from baseline [CFB], -2.2%), FPG 105 mg/dL (CFB, -24 mg/dL), TIR 90% (CFB, +65%).







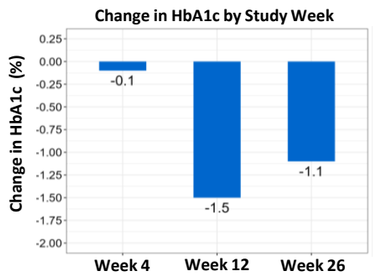


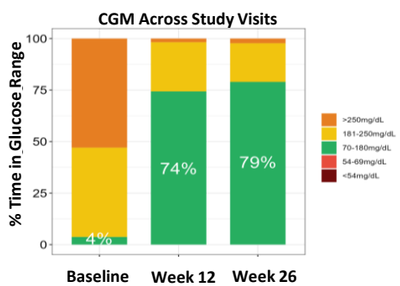
At Week 26, a 29-year-old male participant with a 4-year history of T2D experienced a 2.5% reduction in HbA1c and an increase of 56% TIR compared to baseline after 4 weeks BMF-219 200mg QD without food, indicating a durable effect on glycemic control.

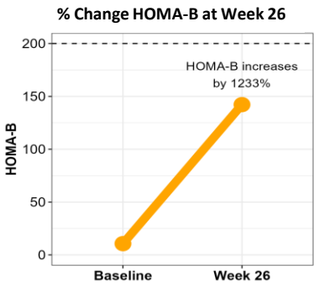
Case Study 2

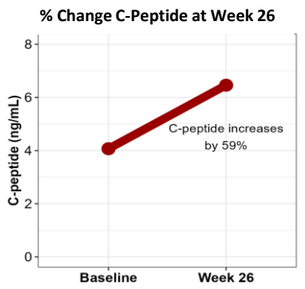
- 45-year-old man with 10-year history of T2D
- Metformin 500 mg BID
- HbA_{1c} 8.6%; FPG 235 mg/dL; BMI 29.6 kg/m^2
- CGM TIR 4%

- BMF-219 100 mg QD with food for 4 weeks
- Metformin continued
- No adverse events reported
- At (Week 26), HbA1c 7.5% (CFB, -1.1%), FPG 144 mg/dL (CFB, -91 mg/dL), TIR 79% (CFB, +73%), HOMA B (CFB, 12-fold increase).









At Week 26, a 45-year-old male participant with 10-year history of T2D experienced a 1.1% reduction in HbA1c and an increase of 75% TIR compared to baseline after 4 weeks BMF-219 100mg QD with food, indicating a durable effect on glycemic control.

Summary and Conclusions

- These case studies illustrate the potential disease-modifying and durable effect of short-term BMF-219 treatment in patients with uncontrolled T2D
- HbA1c and Time-In-Range (TIR) on CGM continue to improve while off treatment
- Increase in HOMA-B and C-peptide correlates with glycemic control, consistent with BMF-219's core mechanism of action: beta-cell proliferation and improved beta-cell function

References

1. Butler T. et al. Oral Long-Acting Menin Inhibitor Normalizes Type 2 Diabetes Mellitus (T2DM) in Two Rat Models. Diabetes 1 June 2022; 71 (Supplement_1): 851–P.
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3. Frias J. et al. BMF-219: A Novel Therapeutic Agent to Re-Establish Functional Beta Cells and Provide Long-Term Glycemic Control. Metabolism May 2023; 142 (Supplement): Abstract #0088

Biomea Fusion sincerely acknowledges and thanks all the COVALENT-111 participants and their families, as well as the site Principal Investigators and staff for their hard work and dedication.