

Improvement of serum lipid panel by Tipelukast (MN-001) in Type 2 Diabetes and NAFLD patients

Abstract # LI2022-1192



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INTRODUCTION

MN-001 (tipelukast) is a novel, orally bioavailable small molecule with anti-inflammatory and anti-fibrotic activity through leukotriene receptor antagonism, phosphodiesterase 3 and 4 inhibition, and 5 lipoxygenase inhibition. In a recent clinical trial (MN-001-NATG-201), MN-001 significantly reduced serum triglycerides (TG) in patients with NAFLD and hypertriglyceridemia (HTG)¹. Moreover, in vitro studies demonstrated that MN-001 downregulates CD36^{2,3} and upregulates ABCG1 mRNA expression, both highly associated with type 2 diabetes mellitus (T2DM).

AIM

To explore MN-001's utility in indications other than NAFLD, a sub-group analysis was conducted in this sample population dual-diagnosed with NAFLD and HTG, and presence of T2DM.

METHODOLOGY

MN-001-NATG-201 was an open-label study to evaluate MN-001's effects on serum TG in subjects who received MN-001 up to 500 mg/day for 12 weeks. Subjects were grouped into 2 categories: with T2DM and without T2DM. The changes in lipid profile, as well as demographic and other baseline characteristics, were assessed.

RESULTS

Subject	All (n=19)	With T2DM (n=10)	Without T2DM (n=9)
Mean Age (y)	54.6	56.7	52.2
Gender Male/Female	8 / 11	4 / 6	4 / 5
Race Caucasian Pacific Islander	18 1	10 0	8 1
Mean Weight (kg)	91.3	92.3	90.2

Mean TG (mg/dL)	Baseline	Week 8	Change	p-value
All Subjects (N=19)	345.7	206.9	-40.2 %	p=0.098
With T2DM (n=10)	444.7	218.7	-50.8%	
Without T2 DM (n=9)	235.7	193.8	-17.8%	

Mean T. cholesterol (mg/dL)	Baseline	Week 8	Change
All Subjects (N=19)	202.9	187.7	-7.5 %
With T2 DM (n=10)	210.2	192.8	-8.3 %
Without T2 DM (n=9)	194.8	182	-6.6 %

RESULTS (cont.)

Mean serum HDL (mg/dL)	Baseline	Week 8	Change	p-value
All Subjects (N=19)	38.7	41.9	+ 8.26 %	p<0.0002
With T2 DM (n=10)	36	41.7	+15.8 %	
Without T2 DM (n=9)	41.8	42.2	+0.96 %	

Mean serum LDL (mg/dL)	Baseline	Week 8	Change
All Subjects (N=19)	118.1	104.4	-11.6 %
With T2 DM (n=10)	126.9	107.4	-15.4 %
Without T2 DM (n=9)	108.3	101	-6.7 %

Compared to subjects without T2DM, the T2DM group showed a trend in reduction of serum TG levels at Week 8 (50.82% versus 17.77%, p=0.098).

Mean HDL increase was significantly greater in subjects with T2DM than subjects without T2DM at Week 8 (15.83% versus 1.05%, p <0.0002).

In comparison to subjects without T2DM, the T2DM group showed a trend in reduction in serum LDL levels at Week 8 (15.37% versus 6.74%).

CONCLUSIONS

The magnitude of changes in serum TG and HDL were substantially greater in the T2DM group than in the non-T2DM group in subjects with NAFLD/HTG comorbidity. These findings suggest that MN-001 is a potential treatment for patients with T2DM, NAFLD who have hypertriglyceridemia. Another trial has commenced to evaluate this phenomenon in patients with T2DM, NAFLD, and HTG (NCT 05464784).

REFERENCES

1. K Matsuda *The International Liver Congress 2018, the 53rd annual meeting of the European Association for the Study of the Liver (EASL)*
2. M Ogura *The Liver Meeting® 2021, the Annual Meeting of the American Association for the Study of Liver Diseases*
3. M Ogura *19th International Symposium on Atherosclerosis (ISA2021)*

DISCLOSURE

Matsuda K, Makhay M, and Iwaki Y are employees of MediciNova, Inc.

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