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PEMVIDUTIDE TREATMENT REDUCES ALCOHOL INTAKE IN A LEAN GOLDEN SYRIAN HAMSTER MODEL

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INTRODUCTION

- Estimated 27.9 million patients in the United States with alcohol use disorder (AUD)[1]
- Up to 90% of patients with AUD develop liver steatosis[2]
- Many patients with AUD progress to alcohol-related liver disease (ALD), characterized by liver inflammation and hepatic fibrosis, if left untreated[3]
- Approximately 2.5% of patients with AUD are treated with medication, and the currently available treatments are limited by undesirable side effects or lack of efficacy[1]
- Data suggests that GLP-1 receptor agonists can reduce alcohol intake, but GLP-1 agonists do not have direct effects on the liver[4]
- Pemvidutide is a balanced 1:1 glucagon/GLP-1 dual receptor agonist in development for the treatment of AUD and ALD[5]
- Preclinical and clinical studies have demonstrated the effect of pemvidutide on hepatic steatosis, inflammation, and fibrosis, potentially important attributes in the treatment of AUD[6]

AIM

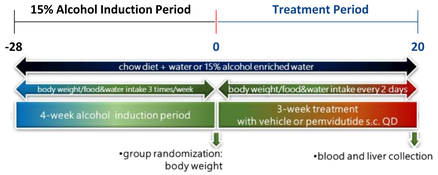
- To evaluate the effects of pemvidutide on alcohol intake in a golden Syrian hamster model
- To evaluate the effects of pemvidutide on alcohol related hepatic gene expression in a golden Syrian hamster model

ACKNOWLEDGEMENTS/ CONTACT INFORMATION

Disclosures: This study was sponsored by Altimmune, inc. MLA, JJS, and MSR are employees of Altimmune, Inc., hold a financial interest in the company, and may own stock / stock options. FB is an employee of Physiogenex and holds a financial interest in the company.

METHODS

- During a 4-week induction period, golden Syrian hamsters were allowed free access to a standard chow diet and normal tap water or 15% alcohol-enriched water
- After the 4-week induction period hamsters were randomized into two treatment groups by bodyweight
- Hamsters were treated once daily with vehicle or pemvidutide 10 nmol/kg subcutaneously for 3 weeks
- Fluid intake and body weight were monitored throughout the study
- RT-qPCR was conducted on liver tissue samples at Day 20



Group	# Animals	Treatment	Treatment Frequency	Dose
1	12	vehicle	1 x Daily	--
2	12	pemvidutide	1 x Daily	10nmol/kg

RESULTS

- Hamsters developed a preference for alcohol over water

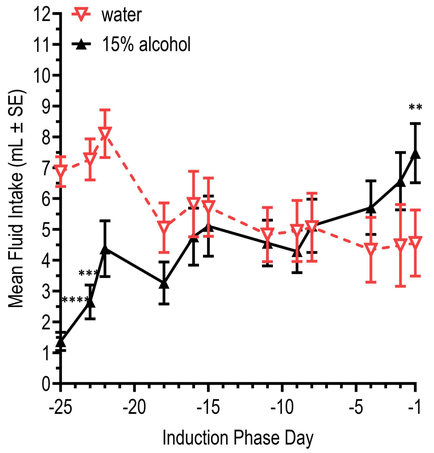


Figure 1. Alcohol intake significantly increased during the induction phase. *Golden Syrian hamsters had a free-choice between normal tap water of 15% alcohol-enriched water for 4 weeks. **p<0.01, ***p<0.001, ****p<0.0001 vs. water (ANOVA 2-way + Bonferonni's post-test)*

- Pemvidutide treatment resulted in a sustained reduction in alcohol intake by Day 3.
- Pemvidutide treatment resulted in a maximal reduction in mean percent alcohol intake of ~80% from treatment initiation

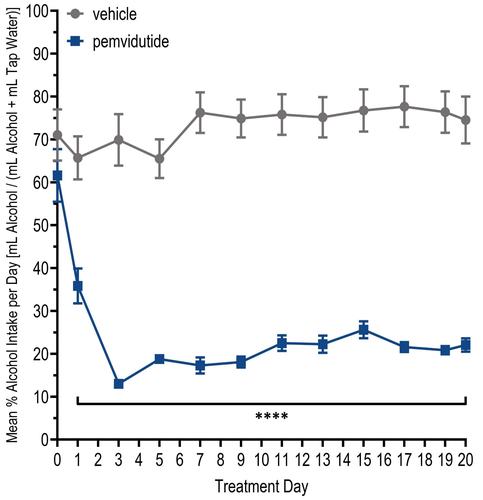


Figure 2. Pemvidutide treatment resulted in significantly reduced alcohol intake. *Mean alcohol intake per day as a percentage of total fluid intake. ****p<0.0001 vs. vehicle (ANOVA 2-Way + Sidak's Multiple Comparison Test). CFB = change from baseline*

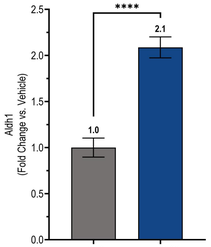


Figure 3. Change in hepatic alcohol metabolism gene expression following pemvidutide treatment. *Aldehyde dehydrogenase 1 (ALDH1). ****p<0.0001 vs. vehicle (Mann-Whitney).*

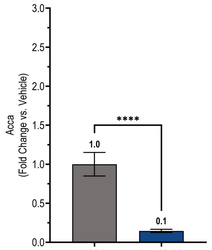


Figure 4. Change in hepatic gene expression for fatty acid synthesis following pemvidutide treatment. *Acetyl-CoA carboxylase 1 (Acca). ****p<0.0001 vs. vehicle (Mann-Whitney).*

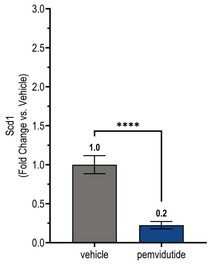


Figure 5. Change in hepatic gene expression for monosaturated fatty acid synthesis following pemvidutide treatment. *Stearoyl-CoA desaturase-1. ****p<0.0001 vs. vehicle (Mann-Whitney).*

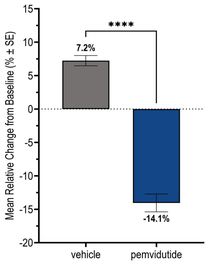


Figure 6. Pemvidutide treatment resulted in significant weight loss. *Relative change in body weight at Day 20. ****p<0.0001 vs. vehicle (t-test).*

CONCLUSIONS

- Pemvidutide treatment significantly reduced alcohol intake in a preclinical hamster model of AUD
- Pemvidutide treatment significantly increased the expression of genes involved in hepatic alcohol metabolism
- Pemvidutide treatment significantly reduced the expression of the pro-apoptotic gene caspase-3 in the liver
- Pemvidutide treatment significantly reduced the expression of hepatic lipogenesis genes
- Pemvidutide treated hamsters lost significantly more weight than vehicle controls

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