Umecrine Cognition presents data supporting a new predictive biomarker in patients with primary biliary cholangitis at the AASLD International Liver Meeting 2021

STOCKHOLM – Umecrine Cognition AB today announces new scientific results for its drug candidate golexanolone, linking the drug target allopregnanolone to cognitive symptoms in patients with primary biliary cholangitis. The data will be presented at The Liver Meeting Digital ExperienceTM 2021, the premier Annual Meeting of the American Association for the Study of Liver Diseases (AASLD), being held November 12-15.

Umecrine Cognition is developing golexanolone, a novel GABAA receptor modulating steroid, which is currently in clinical development for hepatic encephalopathy, and is being considered for development also toward other indications related to the central nervous system. The Liver Meeting Digital Experience™ brings together global actors to exchange information on the latest research, discuss new developments in clinical hepatology, and network with leading experts. At the meeting, Umecrine Cognition will present a scientific poster including results from a recent study of the neurosteroid allopregnanolone in serum samples from 160 subjects with primary biliary cholangitis (PBC) and healthy volunteers conducted in collaboration with the Newcastle University and the UK-PBC organization, UK.

The principal objective of the study was to evaluate the association between allopregnanolone and health related quality of life in PBC patients, using a validated and trusted disease-specific measure for PBC (PBC-40). In the study, serum allopregnanolone levels were analyzed in 160 subjects, including 120 PBC patients and 40 age and gender matched healthy controls. Further, serum allopregnanolone was compared across the PBC-40 domains for those exhibiting no or mild symptoms and those exhibiting severe symptoms.

The study results revealed two key insights. Firstly, elevated serum levels of allopregnanolone were significantly associated with severe cognitive and emotional symptoms ($p=0.02$ and $p=0.004$, respectively) as well as with itch ($p=0.03$). These results align well with what is expected from drug interactions with GABAA receptors. Secondly, the results indicate that younger age was predictive of significantly higher allopregnanolone levels within the PBC cohort ($p < 0.001$), but not in healthy controls ($p = 0.119$). In association, younger age was coupled to more severe cognitive symptoms (severe vs. none; $p = 0.001$) [1].

“This is the first serum marker we have ever seen for fatigue or cognitive symptoms in primary biliary cholangitis. We are now excited to take the next important step into a proof-of-concept intervention study, where a sufficient patient population is available”, says Dr David Jones, Professor of Liver Immunology at Newcastle University and Honorary Consultant Hepatologist at Newcastle’s Freeman Hospital.

While the exact mechanism of non-cirrhotic cognitive dysfunction in PBC remains unknown, elevation of neurosteroids has previously been reported to affect fatigue severity [2]. The company's new findings, to be presented at AASLD, have extended this finding and demonstrates a significant elevation of circulating allopregnanolone in PBC patients with severe cognitive symptoms compared with PBC disease controls, as defined by cut-offs for the cognitive domain in the PBC-40 [3].

"Based on these novel clinical results and other supportive data, the company is preparing for a Phase 2 clinical study. In the study we will assess golexanolone's safety and tolerability profile, its pharmacokinetics, and the clinical effect on quality-of-life-measures including fatigue, sleepiness, and cognitive function in primary biliary cholangitis patients," said Magnus Doverskog, CEO of Umecrine Cognition.

The study results will be presented at The Liver Meeting Digital Experience™ under the topic "Cholestatic and autoimmune liver disease" A link to the abstract can be found here:

https://aasldpubs.onlinelibrary.wiley.com/doi/epdf/10.1002/hep.32188 (no. 1282).

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About Umecrine Cognition AB

Umecrine Cognition's golexanolone (aka GR3027) represents a first-in-class orally active product designed to normalize GABA-ergic transmission, of which allosteric activation by neurosteroids is implicated in several major CNS-related disorders, including HE, a potentially life-threatening disorder with high and growing unmet medical need, and cognitive dysfunction associated with PBC. Golexanolone was shown to inhibit allosteric activation by neurosteroids and normalize GABA-ergic transmission in humans [4]. For more information, please visit www.umecrinecognition.com and see the references below.

About Primary Biliary Cholangitis (PBC)

PBC is an orphan and autoimmune liver disease characterized by destruction of the intra-hepatic bile ducts. Almost a third of patients with primary biliary cholangitis (PBC) experience cognitive symptoms unrelated to cirrhosis (often described as 'brain fog') that can have a significant impact on quality of life (QoL) and there is no effective medical treatment [3]. The mechanistic basis remains poorly understood although elevated levels of neurosteroids has been reported and related to fatigue severity [2]. The neurosteroid allopregnanolone is a potent positive allosteric modulator of GABAA receptors. It is linked to disorders with adverse effects on cognition and memory. Novel compounds targeting allopregnanolone such as golexanolone could potentially offer a new therapy for those with severe symptomatic PBC, satisfying a significant unmet need.

[1] Wetten A, Ogle L, Mells G, Hegade VS, Jopson L, Corrigan M, Palmer J, Johansson M, Doverskog M, Jones DEJ, Dyson JK. Neurosteroid activation of GABAA receptors: a potential treatment target for cognitive symptoms in primary biliary cholangitis? Hepatology, 2021; 74 (Suppl. 1): 769A.

[2] Ahboucha S, Butterworth RF, Pomier-Layrargues G, Vincent C, Hassoun Z, Baker GB. Neuroactive steroids and fatigue severity in patients with primary biliary cirrhosis and hepatitis C. Neurogastroenterol Motil. 2008;20: 671-679.

[3] Phaw, NA., Dyson JK, Mells G., Jones D. Understanding Fatigue in Primary Biliary Cholangitis. Dig. Dis. Sci., 2020;PMID 32851498.

[4] Johansson M et al., GR3027 reversal of neurosteroid-induced, GABA-A receptor-mediated inhibition of human brain function: an allopregnanolone challenge study. Psychopharmacology 2018; 235:1533-1543.

Attachments

Umecrine Cognition presents data supporting a new predictive biomarker in patients with primary biliary cholangitis at the AASLD International Liver Meeting 2021