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^{13}C-Methacetin Breath Test accurately assesses clinically significant portal hypertension in patients with NASH cirrhosis

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BACKGROUND

Determining prognosis for patients with **compensated NASH cirrhosis** using noninvasive tools is a significant unmet need.

Sub-staging of compensated cirrhosis is based on the presence (or absence) of clinically significant portal hypertension (CSPH), as defined by a hepatic venous pressure gradient (HVPG) ≥ 10 mmHg, which is the main predictor of decompensation.

However, measurement of HVPG is invasive and not used routinely.

The ^{13}C-methacetin breath test (MBT) is a non-invasive, non-operator dependent, real-time molecular correlation spectroscopy assay that measures the abundance of $^{13}CO_2$ produced by hepatic cytochrome p450 metabolism of ingested non-radioactive ^{13}C isotope-labeled methacetin in expired breath, using the Exalenz BreathID© MCS System (see **Figure 1**).

MBT has been shown to assess the degree of liver function in patients with cirrhosis and has been shown to correlate with HVPG in mostly viral cirrhosis.

AIM

To investigate the correlation of MBT with HVPG in patients with biopsy-proven compensated NASH cirrhosis.

METHOD

Baseline data was collected from NASH patients screened for the Galectin Therapeutics Phase II clinical trial (NCT02462967) evaluating GR-MD-02 who underwent MBT and HVPG measurement within 19 (±14) days from each other with an average HVPG of 11.3 (±4.6) mmHg.

All patients had cirrhosis and had never had ascites, variceal hemorrhage or encephalopathy. Demographic information, MBT, HVPG results, liver stiffness and lab tests, were collected and analyzed by logistic regression modeling.

Figure 1: **Orally ingested ^{13}C-Methacetin is exclusively metabolized through cytochrome p450 1A2 and $^{13}CO_2$ is exhaled in human breath**

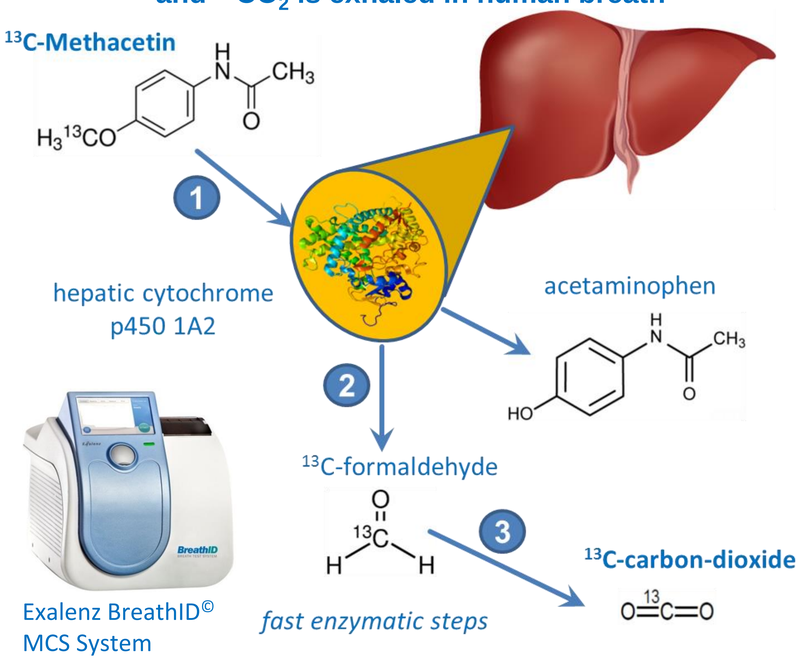


Table1: **Baseline characteristics of analyzed patient population**

Patient population (n= 155)	
Males	53 (34%)
Females	102 (66%)
CSPH	91 (59%)
Age (Mean, SD)	58.3 (8.66) years
BMI (Mean, SD)	34.9 (6.56) kg/m^2

RESULTS

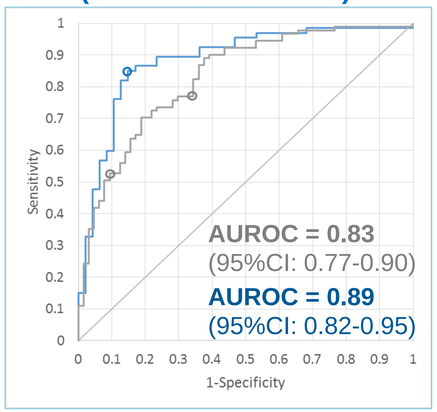
As shown in **Table 1**, the analysis was conducted on 155 patients (53 males; 34%) with 91 (59%) having CSPH. Average age was 58.3 (±8.7) years, with average BMI 34.9 (±6.6) kg/m^2.

Table 2 summarizes the following results: As shown in **Figure 2** the MBT-derived model detected CSPH with an AUROC of 0.83 (95%CI: 0.77-0.90). Selecting two cutoff points in the model (grey circles in **Figure 2**) provide 85% sensitivity and 85% specificity (blue circle in **Figure 2**), CSPH could be ruled in or ruled out in 73.5% of these patients with 89% PPV and 80% NPV, resulting in an AUROC of 0.89 (95%CI: 0.82-0.95). Liver Stiffness as measured by Transient Elastography was available for 120 of the patients and resulted in an AUROC of 0.71 (95%CI: 0.61-0.80). Platelet count and APRI showed an AUROC of 0.76 (95%CI: 0.68-0.83) and 0.71 (95%CI: 0.63-0.80), respectively.

Table2: **AUROC for detection of CSPH**

Measure	AUROC	95% CI
Platelets	0.76	0.68-0.83
APRI	0.71	0.63-0.80
Liver Stiffness as measured by Transient Elastography	0.71	0.61-0.80
MBT-derived model	0.83	0.77-0.90
MBT-derived model after applying two cut-offs	0.89	0.82-0.95

Figure 2: **ROC for the MBT-derived model before and after applying two cut-offs (marked with circles)**



CONCLUSIONS

MBT non-invasively detects CSPH with high sensitivity and specificity, and may serve as a useful tool in the stratification of patients with compensated NASH cirrhosis at point-of-care.

DISCLOSURES

This study is sponsored by Galectin Therapeutics Inc.
PGT is CEO and CMO of Galectin Therapeutics Inc.
YI is Medical Director of Exalenz Bioscience Ltd.