A prospective study to evaluate the efficacy of a standardized low calorie diet according to PNPLA3 genotype in patients with Non Alcoholic Fatty Liver Disease (NAFLD) – 2 months data (interim analysis)

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Background

With a prevalence of 30% in the Western population, NAFLD is one of the most common liver diseases which also increases the risk of Non Alcoholic Steatohepatitis (NASH), fibrosis, cirrhosis and even hepatocellular carcinoma. NAFLD is also referred to as hepatic manifestation of the metabolic syndrome and therefore is strongly associated with the aggravation of diabetes and cardiovascular disease. PNPLA3 is a major risk factor for hepatic steatosis. Especially G allele increases liver fat content and leads to a higher susceptibility for disease progression. Lifestylemodification through dietary and exercise interventions with the main objective of weight reduction represents the cornerstone for treating patients with NAFLD. HEPAFAST® is a protein shake, developed for the treatment of fatty liver disease. Besides whey protein HEPAFAST® is characterized by the addition of different liver protective substances, such as ß-glucan, cholin, taurin and long-chained omega-3-fatty acids.

Aim

Aim of this study is to analyze the efficacy of a standardized low calorie protein shake diet (HEPAFAST®, Bodymed, Kirkel, Germany) specifically developed for patients with NAFLD and the influence of PNPLA3 genotypes on treatment outcome.

Preliminary Results

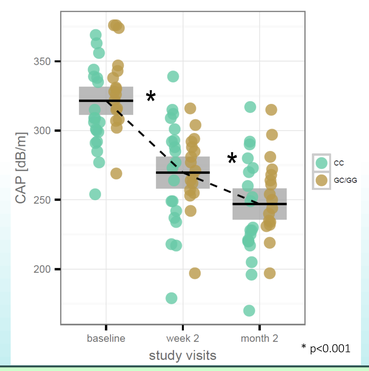
To date 47 patients (age 46.0±8.8 [MW±STABW]; m:28, w:19; PNPLA3: CC:20, CG:20, GG:7) finished the HEPAFAST® shake therapy from baseline to week 2.

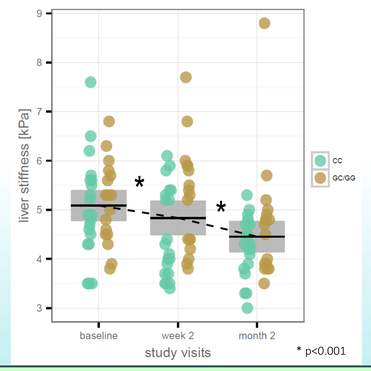
Week 2 analysis: The two-week HEPAFAST® shake therapy results in a significant reduction of CAP (dB/m), liver stiffness (kPa), waist circumference (cm), BMI (kg/m²), fatty liver index (FLI), triglycerides (mg/dl) and GGT (U/l). Additionally, a significant increase of vitamin D (ng/ml) is seen.

Furthermore, 36 patients (age 46.3±9.2 [MW±STABW]; m:24, w:12; PNPLA3: CC:19, CG:11, GG:6) also completed 6 weeks of LOGI diet following HEPAFAST® shake therapy.

Month 2 analysis: Further improvements are obtained for CAP, liver stiffness, waist circumference, BMI and vitamin D after implementing a low glycemic and insulinemic diet for 6 weeks.

Overall, no significant difference is indicated according to PNPLA3 genotype for Fibroscan® CAP, waist circumference, BMI, FLI, triglycerides, GGT and vitamin D. Relating to liver stiffness there seems to be a trend for a better response of patients with CC genotype.



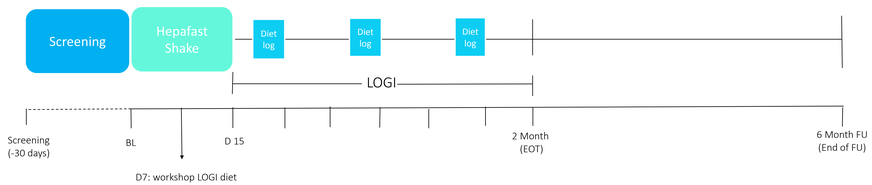


A significant reduction of CAP and liver stiffness is shown from baseline to week 2 and until 2 months visit

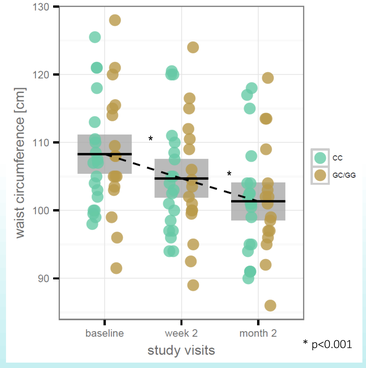
PNPLA3	CC (bl) n=20	CC (w2) n=20	CC (m2) n=19	CG/GG (bl) n=25	CG/GG (w2), n=25	CG/GG (m2), n=17	CC (Δ) bl-w2	CG/GG (Δ) bl-w2	P-value	CC (Δ) bl-m2	CG/GG (Δ) bl-m2	P-value
CAP	310.8±29.3	268.7±40.1	238.2±33.1	322.9±28.0	272.0±28.5	252.6±29.0	42.1±34.5	50.9±30.7	0.59	74.0±30.1	77.3±27.6	0.91
kPa	5.4±1.2	4.4±0.9	4.2±0.6	5.1±1.2	4.9±1.1	4.7±1.2	0.7±1.2	0.8±0.8	0.09	0.8±1.0	0.4±1.0	0.35
FLI	79.1±16.2	58.8±19.4	59.1±19.8	75.6±17.6	54.5±23.5	52.7±24.3	20.4±11.1	21.1±12.9	0.55	19.5±13.1	21.9±13.6	0.32
WC	108.2±8.0	104.7±8.3	101.1±8.7	107.9±9.5	104.4±9.1	101.6±8.4	3.4±1.8	3.6±1.3	0.78	7.2±2.9	7.0±2.6	0.74
BMI	32.2±3.5	30.8±3.3	29.9±3.4	31.3±3.8	29.8±3.5	28.8±3.3	1.4±0.5	1.6±0.6	0.19	2.4±0.9	2.5±0.9	0.42
TG	125.3±70.5	74.9±34.0	97.9±29.7	133.0±53.3	82.2±42.4	117.3±67.4	50.4±54.9	50.8±57.8	0.92	27.6±68.3	15.5±39.3	0.53
GGT	50.7±33.8	30.6±17.4	34.4±25.4	43.3±35.2	27.8±16.3	24.8±13.2	20.1±18.3	15.4±21.5	0.29	13.8±15.1	13.1±15.0	0.83
Vit D	23.4±10.6	27.4±10.9	29.3±10.9	20.1±5.9	22.6±6.2	25.8±5.9	4.0±3.3	2.5±2.7	0.36	6.5±3.9	4.6±5.4	0.47

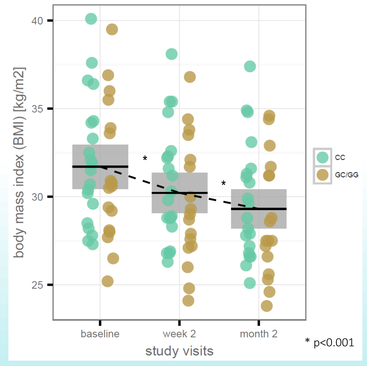
Methods

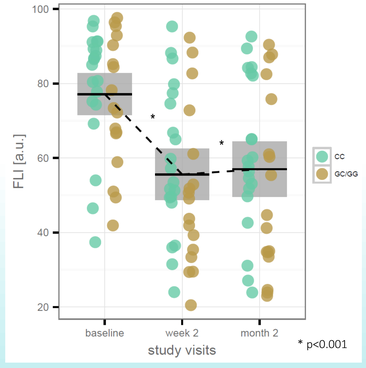
In this study 81 non cirrhotic patients are included and stratified according to PNPLA3 genotype (27 patients per group; CC, CG, GG). All patients receive a low calorie diet (max. 1000kcal per day) with HEPAFAST® protein shakes for 2 weeks and subsequently follow a low glycemic and insulinemic (LOGI) diet for another 6 weeks (EOT). Compliance is monitored with food logs. All patients are seen longitudinally for four time points (baseline, week 2, month 2, 6 months-follow up). Liver fat content measured by Fibroscan® CAP is used as primary endpoint.

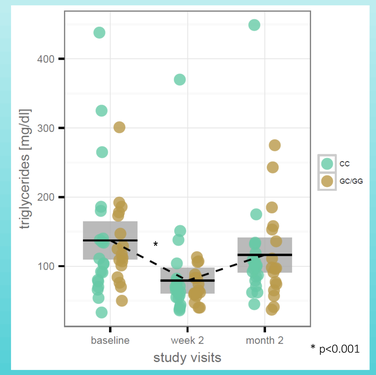


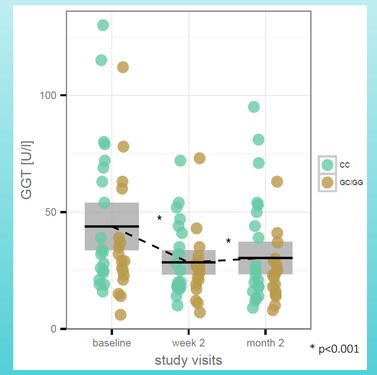
Liver fat content is assessed by an independent/blinded investigator with Fibroscan® CAP at each study visit. Additionally liver stiffness (kPa), fatty liver index (FLI), waist circumference (WC), BMI, triglycerides (TG), GGT and vitamin D are analyzed.

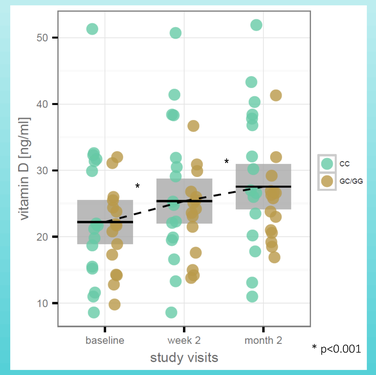












Conclusion: A low calorie diet with HEPAFAST® shakes is a very effective strategy to significantly lower liver fat content in NAFLD patients. Furthermore it leads to a significant drop of liver stiffness. Implementation of a „low glycemic and insulinemic diet“ (LOGI) further improves results. There seems to be no better response to a standardized low calorie diet in patients carrying the PNPLA3 G-allele.

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