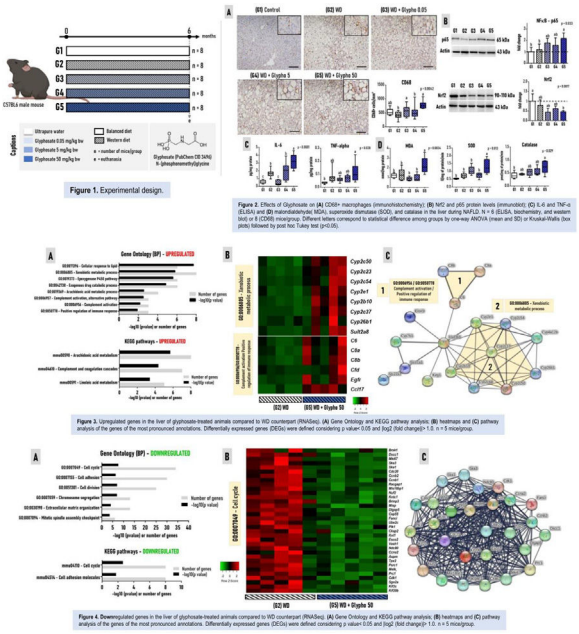
Moreover, Glypho downregulated key “cell cycle”-related genes (as Mki67 and Cdk1).

**Conclusions:** In essence, our results are innovative on demonstrating that Glypho – in a dose within the regulatory limits – impaired the hepatic inflammation/redox dynamics at the morphological, biochemical and transcriptomic levels.



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## O-20 EFFECTS OF ISOCALORIC AND NEGATIVE CALORIE BALANCE EXERCISE ON SERUM LEVELS OF INSULIN-LIKE GROWTH FACTOR TYPE 1 IN SUBJECTS WITH INITIAL AND ADVANCED FATTY LIVER

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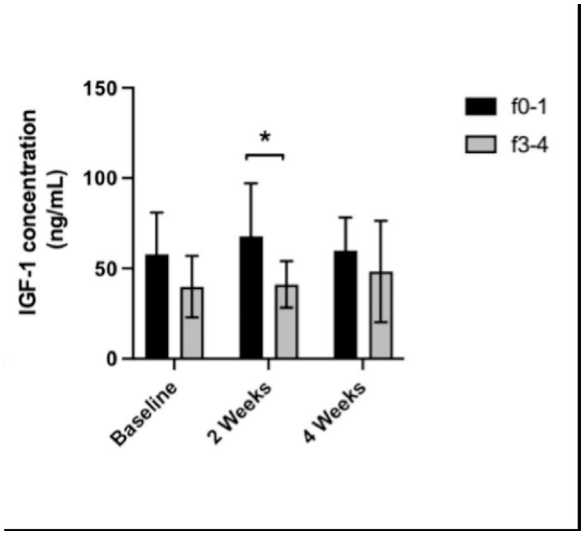
**Introduction and Objectives:** Insulin-like growth factor 1 (IGF-1) is a hepatokine that has a protective effect on fatty liver. Previous studies in healthy subjects suggest that isocaloric exercise (with neutral caloric balance) would increase serum levels of IGF-1. This study aimed to evaluate the effect of moderate isocaloric exercise (ICBE) and negative caloric balance exercise (NCBE) on serum levels of IGF-1 in subjects with initial and advanced (F3-4) MAFLD (Metabolic Associated Fatty Liver Disease).

**Materials and Methods:** Prospective trial in postmenopausal women undergoing supervised and standardized exercise at moderate intensity (1 hour, 3 times per week). The study includes subjects with initial MAFLD (F0-2 Fibroscan <8 kPa) and advanced MAFLD (F3-4, Fibroscan >8 kPa). The protocol consisted of an initial two-week period of ICBE (with nutritional supplement) followed by two weeks of NCBE (without supplement). Using the t-student test for paired samples, the change was analyzed pre vs. post-protocol, and the comparison between groups used the analysis for unpaired samples.

**Results:** We recruited 27 subjects (20 non-advanced MAFLD and 7 advanced MAFLD). We demonstrated that: (1) Exercise did not significantly increase IGF-1 levels in MAFLD; (2) There was a tendency for subjects with initial MAFLD to have higher IGF-1 levels than subjects with advanced MAFLD before and after exercise, which became significant after 2 weeks of exercise (F0-2 67.9 + 6.4 (ng/mL) versus F3-4 41.2 + 5.3 (ng/mL), p 0.047); and (3) There were no significant differences in IGF-1 levels between ICBE and NCBE (figure 1).

**Conclusions:** Subjects with advanced MAFLD tend to have lower IGF-1 levels than subjects with initial MAFLD, which becomes significant after 2 weeks of exercise. This suggests that the response to exercise in terms of changes in hepatokines (IGF-1) varies depending on the stage of the disease.

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## O-21 NUTRITIONAL SUPPLEMENTATION WITH MEXICAN FOODS, OPUNTIA FICUS INDICA, THEOBROMA CACAO, AND ACHETA DOMESTICUS IMPROVED GUT-LIVER AXIS IN A MAFLD MICE MODEL.

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**Introduction and Objectives:** Metabolic-associated fatty liver disease (MAFLD) is the most common liver disease worldwide, several studies have shown that gut microbiota had a strong impact in MAFLD developing. This study aimed to evaluate the effect of a supplementation with a mixture of Mexican foods (MexMix): nopal, cacao and cricket on gut-liver axis.

**Materials and Methods:** Thirty C57BL/6J male mice were divided into three groups: 1) control group: normal diet. 2) HF group: high fat diet (60%) and water with sucrose and fructose and 3) MexMix group (MexMix): HF diet until week 10 and for 8 additional weeks; HF diet pellets supplemented with 6.7% nopal, 8.7% cocoa and 8.7% cricket.

**Results:** Mice treated with MexMix decreased body weight, visceral and epididymal fat, and adipocyte size, as well as serum levels of triglycerides, insulin, leptin, and PAI-1; while adiponectin levels increased. Using 16S rRNA gene sequencing, MexMix was shown to increase phylogenetic diversity, Firmicutes abundance, and enrichment of 10 genera, including Lachnospiraceae, Ruminococcaceae, Akkermansia, and Eubacterium_coprostanoligenes_group, associated with multiple beneficial effects such as short-chain fatty acids (SCFAs) production. In the gut, MexMix supplementation increased significantly fecal SCFAs concentration, intestinal crypts depth, Ocln and Cldn1 expression, and decreased Il6 and Tnf-a expression. In liver, MexMix significantly reduced steatosis. Liver transcriptome in MexMix group showed an enrichment in histone H3K14 acetylation pathway. Using qPCR, we confirmed higher hepatic expression of Cat, Sod and lower expression of Tnfa and Pparg. In addition, MexMix diet decreased hepatic expression of miRNA-34a, miRNA-103, and miRNA-33a.

**Conclusions:** Supplementation with MexMix demonstrated its efficacy as a prebiotic, promoting growth of beneficial genera improving intestinal health. This suggests that MexMix could be a potential therapeutic strategy for treating MAFLD in patients, as well as other conditions linked to excessive consumption of fats and sugars.

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## O-22 EFFICACY OF ATEZOLIZUMAB BEVACIZUMAB TREATMENT FOR HEPATOCELLULAR CARCINOMA IN REAL-WORLD CLINICAL PRACTICE AT TWO TERTIARY HEALTHCARE CENTERS IN SOUTHERN BRASIL: FIRST INTERIM ANALYSIS

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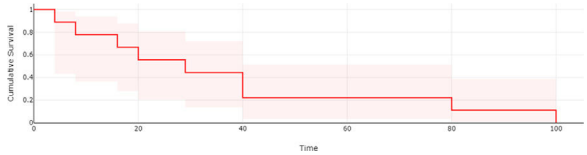
**Introduction and Objectives:** Atezolizumab and bevacizumab (Atez/Bev) are the new standard of care for first-line systemic therapy of hepatocellular carcinoma (HCC). Real-world data on safety and efficacy of Atez/Bev are scarce in Latin America. We aimed to describe safety and efficacy of Atez/Bev in patients with HCC Barcelona Clinic Liver Cancer (BCLC) B and C stages.

**Materials and Methods:** Prospective cohort study at two tertiary healthcare centers in Porto Alegre, Southern Brazil, included consecutive HCC patients within BCLC B or C stages started with Atez/Bev as first line therapy between 2020-2023. Demographics, tumor response, overall survival (OS), and adverse events were assessed.

**Results:** A total of 20 patients, 16 males (80%), all with cirrhosis (HCV 13, HBV 3, NASH 3, alcohol 1). Child-Pugh were A and B (17 and 3, respectively). Median MELD was 8 (IQR 7-10.5) and median age 70.5 years-old (IQR 61-72.8). Median baseline alfa-fetoprotein was 36.8 (IQR 6.6-2.696). Esophageal varices in 11 individuals (65%). Majority (19/20) was BCLC stage C and ECOG 0/1. Previous HCC treatment was surgery (n=2, 10%), radiofrequency ablation (n=1, 5%) or transarterial chemoembolization (n=10, 50%). Macrovascular invasion and extra-hepatic metastasis were detected in 9 (45%) and 5 (25%) patients, respectively. Median Atez/Bev cycles were 5.5 (IQR 3-8.8) and dose reduction occurred in 5 patients (25%). Tumor response was evaluated in 13 patients: partial response in 3 (23.1%), stable disease in 1 (7.6%), and progressive disease in 9 (69.3%). Median follow-up (last visit or death) was 31.5 weeks (IQR 16-47.5). Median OS was 55% (Fig 1). Cirrhosis decompensation occurred in 11/20 individuals (55%) with variceal bleeding in 5/20 (25%), which was the only significant variable associated with mortality (p=0.04).

**Conclusions:** Atez-Bev in a real-world cohort of intermediary and advanced HCC patients showed efficacy and safety comparable to published studies with similar inclusion criteria.

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## O- 23 STRATEGIES TO ELIMINATE HEPATITIS C VIRUS INFECTION IN THE AMERICAS

Luis Antonio Díaz[1], Sergio García[1], Rayan Khan[2], Gustavo Ayares[1], Javier Uribe[1], Francisco Idalsoaga[1], José Miguel Fuentealba[3], Eduardo Fuentes[1], Katherine Maldonado[4], Mariana Lazo[5], Catterina Ferreccio[1], Manuel Mendizabal[6], Melisa Dirchwolf[7], Patricia Guerra[8], Claudia P. Oliveira[9], Mario Guimarães[9], Mario Reis[10], Giada Sebastiani[11], Mayur Brahmania[12], Alnoor Ramji[13], Mina Niazi[14], Hin Hin Ko[13], Jordan Feld[15], Juan Carlos Restrepo[16], Wagner Ramírez[17], Omar Alfaro[18], Marlen Castellanos-Fernández[19], Enrique Carrera[20], José Roberto Aguirre Ayala[21], Abel Sánchez[4], Marco Sánchez[22], María Teresa Andara[23], Graciela Castro[24], Norberto Chavez-Tapia[25], Nahum Mendez-Sanchez[25], Enrique Adames[26], Julissa Lombardo[27], Marcos Girala[28], Elías Morán[28], Martin Padilla-Machaca[29], Javier Díaz[30], Martín Tagle[31], Victoria Mainardi[32], Nelia Hernandez[33], Edmundo Martínez[34], Edilmar Alvarado-Tapias[35], Roberto Leon[36], Andrew Talal[37], Emmanuel Thomas[38], Sandra Springer[39], Mauricio Garcia-Saenz-de-Sicilia[40], Wei Zhang[41], Jasmohan Bajaj[42], Elliot B. Tapper[43], Manhal J. Izzy[44], Robert G. Gish[45], Bashar Attar[46], Thomas G. Cotter[47], Michael R. Lucey[48], Patrick S. Kamath[49], Ashwani K. Singal[50], Ramón Bataller[51], Gabriel Mezzano[52], Alejandro Soza[1], Jeffrey V. Lazarus[53], Marco Arrese[1], Juan Pablo Arab[2]

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