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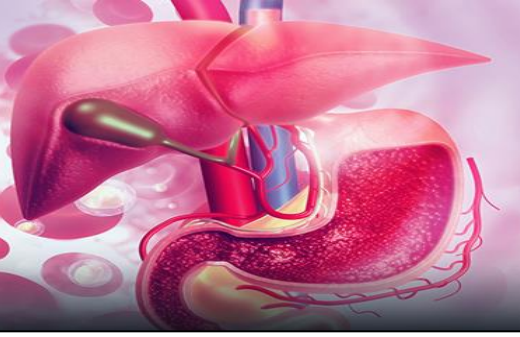

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "ENTERON" which contains latest and interesting news in the field of Gastroenterology.

Inside This Issue:

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

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Delayed lower intestinal bleeding after organophosphate poisoning: A case report

Background:

Poisoning by organophosphates (OP) is a substantial public health problem in underdeveloped countries, with significant casualties. Although gastrointestinal (GI) bleeding is not a common symptom of OP poisoning, some cases have suggested that it can be serious and even fatal. Although technology advancements have made detecting GI bleeding more efficient and precise, diagnosing and treating the underlying cause still takes days in most cases.

Objective:

This study presented an unusual instance and a treatment plan that may aid clinicians in recognising the diversity of symptoms in OP poisoning and providing more effective therapy to patients.

Case Presentation:

A 78-year-old woman was taken to the hospital about 12 hours after attempting suicide by consuming a mouthful of organophosphate and benzodiazepines. She experienced reoccurring melena six weeks after receiving successful medical treatment for respiratory failure. The results of colonoscopy and esophagogastroduodenoscopy revealed no ulcers or bleeding. Enteroscopy revealed extensive circumferential ulcers 10 cm proximal to the ileocecal valve, as well as luminal constriction. After failing medical treatment, the patient underwent a 100-cm ileum resection and recovered normally. Around 50 cm proximal to the ileocecal valve, the excised terminal ileum revealed significant inflammation and a distinct transitional zone between the healthy and wounded mucosa. A damaged mucosa with inflammatory cell infiltrate and structural damage was discovered on pathological testing. This case demonstrates an uncommon occurrence of OP poisoning with late-onset lower gastrointestinal bleeding, which slowed the patient's recovery and required parenteral hydration.

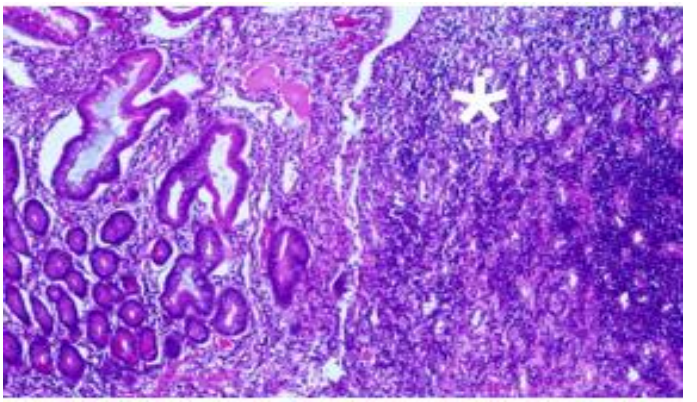

Figure 1: The transitional zone with a sharp and obvious margin. The injured mucosa with inflammation and stenosed tissue is marked

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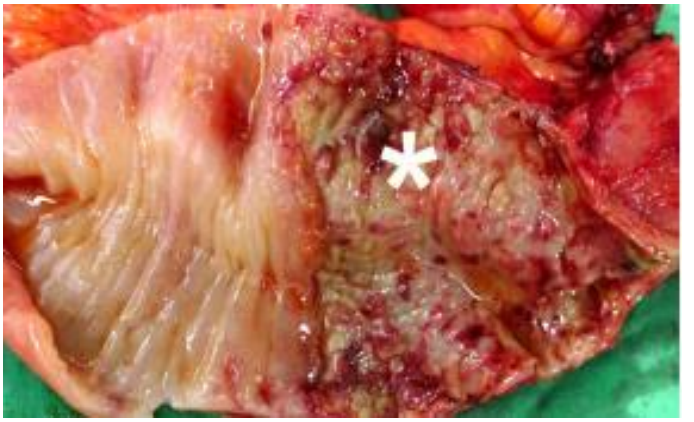

Figure 2: The transitional zone under 40×10 magnification with hematoxylin and eosin (HE) stain. The injured mucosa is marked. The right side of the picture denotes the relatively healthy mucosa with the gland tissue still preserved

Conclusion:

This case described an unusual case of OP poisoning that resulted in late-onset lower GI tract bleeding, which significantly lengthened the patient's recovery and parenteral alimentation period. Apart from SLUDGE symptoms, special attention should be made to OPs that cause digestive problems and ensure that the problem is adequately addressed in a timely manner.

Reference:

Hung W, Tsai TH, Chen JH. A case report of delayed lower intestinal bleeding after organophosphate poisoning. BMC Gastroenterol. 2021 Oct 29;21(1):414.

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A systematic review and meta-analysis evaluating the impact of medicinal therapy for inflammatory bowel illness on the severity of COVID-19

Background:

Long-term maintenance pharmacological therapy, such as 5-aminosalicylic acid (5-ASA), immunomodulators, janus kinase (JAK) inhibitors, biologic medicines, or corticosteroids, is often required for patients with inflammatory bowel disease (IBD). The impact of these drugs on the COVID-19 outcome is unknown. The SECURE-IBD database is an international registry that was developed at the start of the COVID-19 pandemic for documenting COVID-19 outcomes in patients with IBD.

It now has the results of over 6000 patients with IBD who have COVID-19 infection from 72 countries throughout the world. Furthermore, many studies have been conducted to assess the safety of IBD drugs during the COVID-19 epidemic, with mixed results. There had never been a systematic analysis of individual biologic therapy and the risk of severe COVID-19 before. Furthermore, this is the first and largest systematic review to cover anti-TNF and janus kinase inhibitors.

Objective:

To evaluate the link between IBD treatments and severe COVID-19 outcomes.

Methods:

A systematic review and metaanalysis of all published studies from December 2019 to August 2021 was conducted to find studies that reported severe COVID-19 outcomes in patients receiving current IBD treatments such as 5-aminosalicylic acid (5-ASA), immunomodulators, corticosteroids, biologics, combination therapy, or tofacitinib.

Results:

There were twenty-two studies found. In individuals with IBD, corticosteroids (RR 1.91 (95 percent CI 1.25 to 2.91, p=0.003)) and 5-ASA (RR 1.50 (95 percent CI 1.17 to 1.93, p=0.001) were linked to an elevated risk of severe COVID-19 outcomes. However, any confounders associated with the usage of 5-ASA were not taken into account. Corticosteroids increased the likelihood of ICU admission but not of mortality, according to a sub-analysis.

Tofacitinib and vedolizumab were not linked with severe disease when used alone or in conjunction with anti-TNFs (RR 0.96 (95 percent CI 0.80 to 1.15, p Anti-TNFs (RR 0.47 (95 percent CI 0.40 to 0.54, $p < 0.00001$) and ustekinumab (RR 0.55 (95 percent CI 0.43 to 0.72, $p < 0.00001$) were linked to a lower incidence of severe COVID-19

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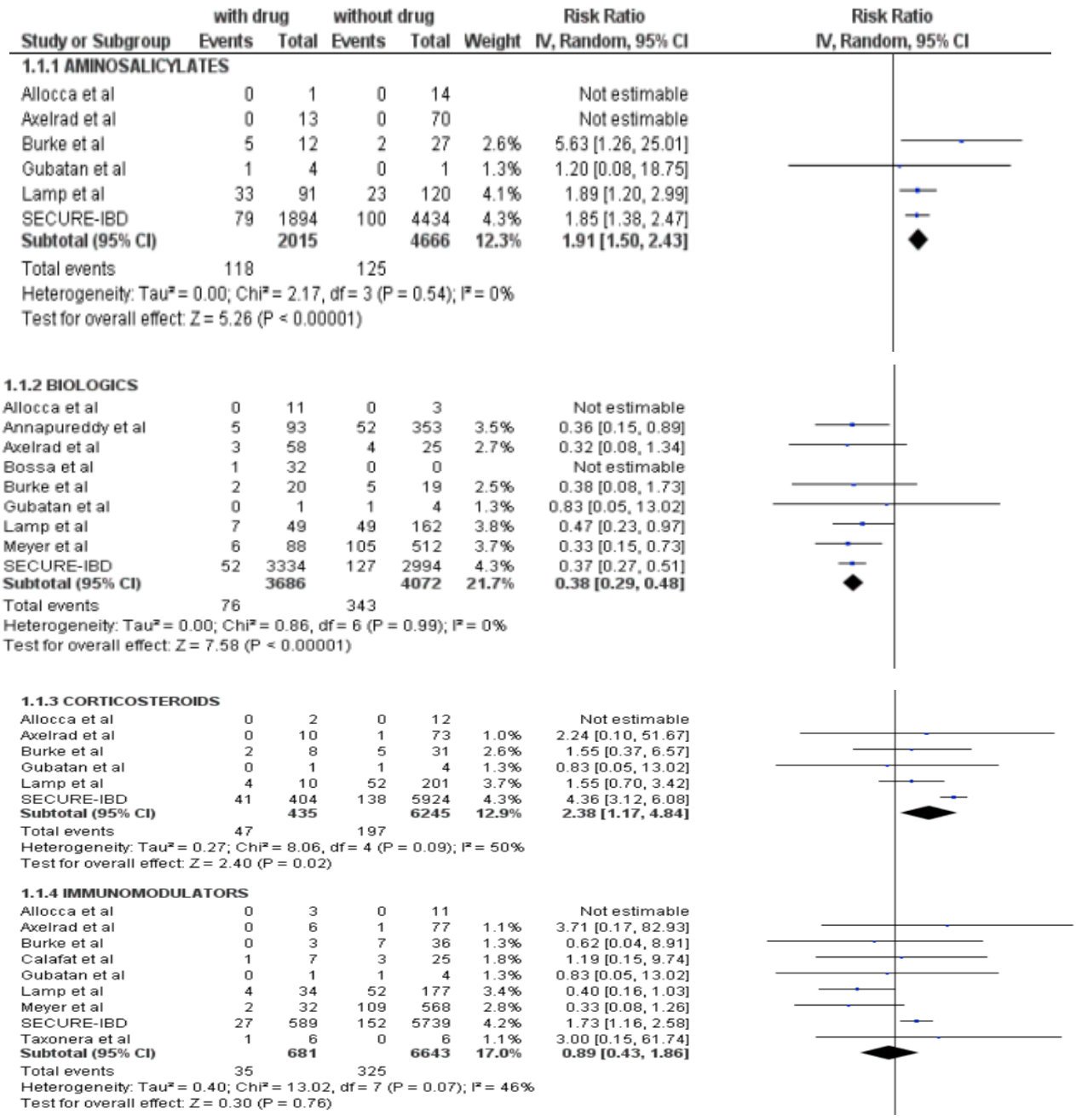

Study or Subgroup	with drug Events	Total	without drug Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 AMINOSALICYLATES						
Allocca et al	0	1	0	14		Not estimable
Axelrad et al	0	13	0	70		Not estimable
Burke et al	5	12	2	27	2.6%	5.63 [1.26, 25.01]
Gubatan et al	1	4	0	1	1.3%	1.20 [0.08, 18.75]
Lamp et al	33	91	23	120	4.1%	1.89 [1.20, 2.99]
SECURE-IBD	79	1894	100	4434	4.3%	1.85 [1.38, 2.47]
Subtotal (95% CI)		**2015**		**4666**	**12.3%**	**1.91 [1.50, 2.43]**
Total events	118		125			
Heterogeneity: Tau² = 0.00; Chi² = 2.17, df = 3 (P = 0.54); I² = 0%						
Test for overall effect: Z = 5.26 (P < 0.00001)						
1.1.2 BIOLOGICS						
Allocca et al	0	11	0	3		Not estimable
Annapureddy et al	5	93	52	353	3.5%	0.36 [0.15, 0.89]
Axelrad et al	3	58	4	25	2.7%	0.32 [0.08, 1.34]
Bossa et al	1	32	0	0		Not estimable
Burke et al	2	20	5	19	2.5%	0.38 [0.08, 1.73]
Gubatan et al	0	1	1	4	1.3%	0.83 [0.05, 13.02]
Lamp et al	7	49	49	162	3.8%	0.47 [0.23, 0.97]
Meyer et al	6	88	105	512	3.7%	0.33 [0.15, 0.73]
SECURE-IBD	52	3334	127	2994	4.3%	0.37 [0.27, 0.51]
Subtotal (95% CI)		**3686**		**4072**	**21.7%**	**0.38 [0.29, 0.48]**
Total events	76		343			
Heterogeneity: Tau² = 0.00; Chi² = 0.86, df = 6 (P = 0.99); I² = 0%						
Test for overall effect: Z = 7.58 (P < 0.00001)						
1.1.3 CORTICOSTEROIDS						
Allocca et al	0	2	0	12		Not estimable
Axelrad et al	0	10	1	73	1.0%	2.24 [0.10, 51.67]
Burke et al	2	8	5	31	2.6%	1.55 [0.37, 6.57]
Gubatan et al	0	1	1	4	1.3%	0.83 [0.05, 13.02]
Lamp et al	4	10	52	201	3.7%	1.55 [0.70, 3.42]
SECURE-IBD	41	404	138	5924	4.3%	4.36 [3.12, 6.08]
Subtotal (95% CI)		**435**		**6245**	**12.9%**	**2.38 [1.17, 4.84]**
Total events	47		197			
Heterogeneity: Tau² = 0.27; Chi² = 8.06, df = 4 (P = 0.09); I² = 50%						
Test for overall effect: Z = 2.40 (P = 0.02)						
1.1.4 IMMUNOMODULATORS						
Allocca et al	0	3	0	11		Not estimable
Axelrad et al	0	6	1	77	1.1%	3.71 [0.17, 82.93]
Burke et al	0	3	7	36	1.3%	0.62 [0.04, 8.91]
Calafat et al	1	7	3	25	1.8%	1.19 [0.15, 9.74]
Gubatan et al	0	1	1	4	1.3%	0.83 [0.05, 13.02]
Lamp et al	4	34	52	177	3.4%	0.40 [0.16, 1.03]
Meyer et al	2	32	109	568	2.8%	0.33 [0.08, 1.26]
SECURE-IBD	27	589	152	5739	4.2%	1.73 [1.16, 2.58]
Taxonera et al	1	6	0	6	1.1%	3.00 [0.15, 61.74]
Subtotal (95% CI)		**681**		**6643**	**17.0%**	**0.89 [0.43, 1.86]**
Total events	35		325			
Heterogeneity: Tau² = 0.40; Chi² = 13.02, df = 7 (P = 0.07); I² = 46%						
Test for overall effect: Z = 0.30 (P = 0.76)						

Table 1: Forest plot showing the risk of intensive care unit (ICU) admission in patients taking 5-ASA, biologics, corticosteroids, immunomodulators

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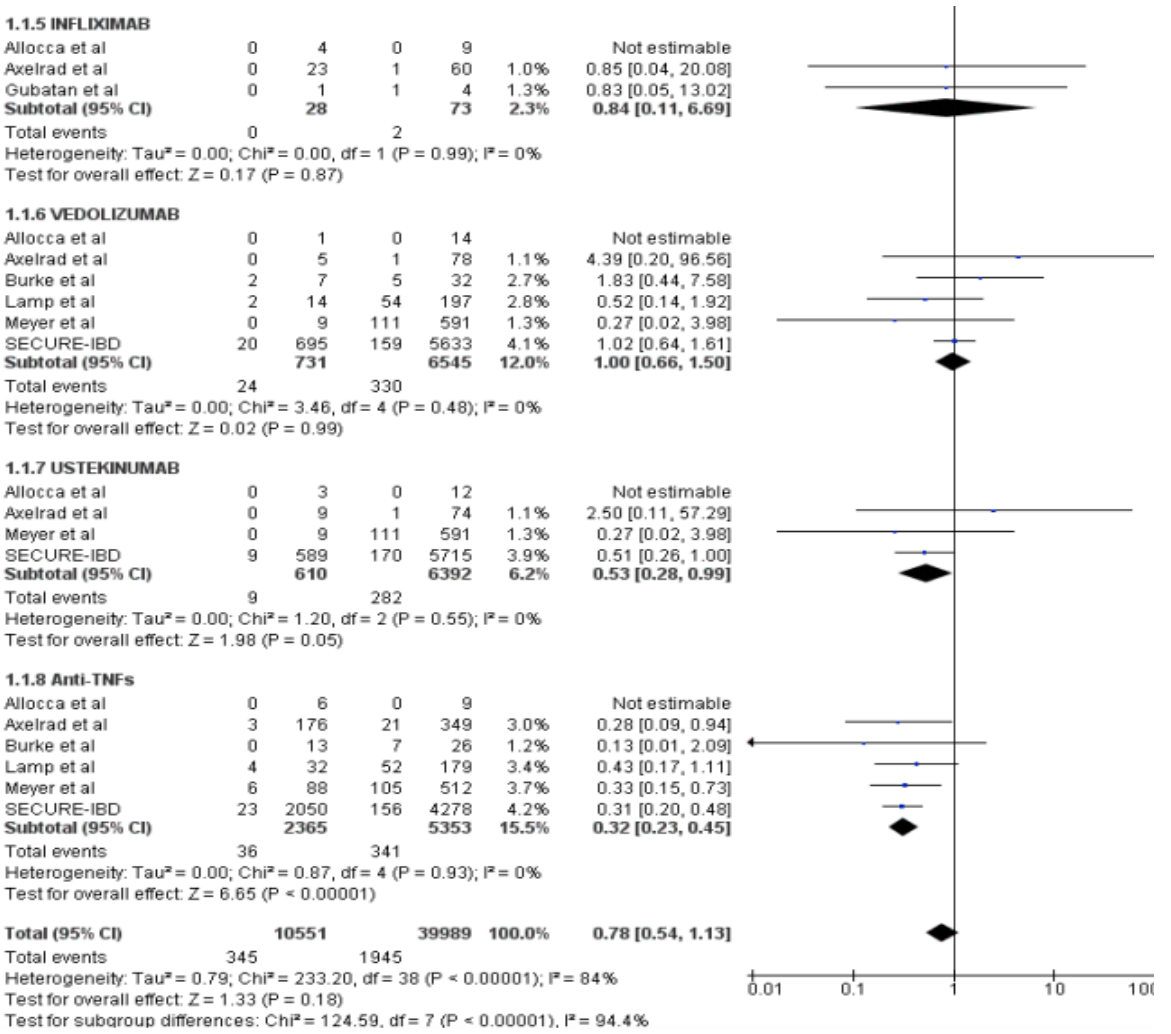

Table 2: Forest plot showing the risk of intensive care unit (ICU) admission in patients taking infliximab, vedolizumab, ustekinumab and anti-TNFs

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Conclusion:

Patients with IBD who take corticosteroids have a greater risk of developing severe COVID-19. ICU admission was linked to corticosteroid use, but not mortality. Patients using 5-ASAs are likewise at a higher risk. However, patient-level data was limited, and meta-regression studies to correct for confounding were not possible due to a lack of data.

Vedolizumab, tofacitinib, and immunomodulators were not linked to severe illness whether used alone or in combination with anti-TNF. Anti-TNFs and ustekinumab were linked to positive results.

Reference:

Alrashed F, Battat R, Abdullah I, Charabaty A, Shehab M. Impact of medical therapies for inflammatory bowel disease on the severity of COVID-19: a systematic review and meta-analysis. BMJ Open Gastroenterol. 2021 Oct;8(1):e000774.

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FASCINATE-1, a Randomized, Placebo Controlled Phase 2a Trial of TVB-2640 (FASN Inhibitor) for the Treatment of Nonalcoholic Steatohepatitis

Background:

Nonalcoholic fatty liver disease (NAFLD) refers to a variety of liver diseases that proceed from simple steatosis to nonalcoholic steatohepatitis (NASH) without fibrosis, NASH with fibrosis, and, eventually, cirrhosis.

Increased intrahepatic fat and the production of lipotoxic metabolites damage hepatocytes, stimulate inflammatory responses, and activate profibrotic stellate cells in the liver, which start and drive the course of NAFLD. The de novo lipogenesis (DNL) pathway, which involves the enzymes acetyl-CoA-carboxylase (ACC) and fatty acid synthase (FASN) converting metabolites of simple dietary sugars into the fatty acid palmitate, is important in the formation of excess fat in the liver and the generation of lipotoxic molecules. Insulin resistance and blood glucose levels in NAFLD patients may promote DNL even more, resulting in higher intrahepatic triglyceride levels. In nonalcoholic steatohepatitis, increased de novo lipogenesis produces excess intrahepatic fat and lipotoxins, perpetuating liver damage. A fatty acid synthase inhibitor, TVB-2640, was developed to remove excess liver fat while also inhibiting inflammatory and fibrogenic pathways directly.

Objective:

This study aimed to evaluate the safety and efficacy of TVB-2640 in patients with nonalcoholic steatohepatitis in the United States.

Methods:

A single-blind, randomised, placebo-controlled study. Adults with 8% liver fat, as measured by magnetic resonance imaging proton density fat fraction, and evidence of liver fibrosis, as measured by magnetic resonance elastography 2.5 kPa or liver biopsy, were included in the study. Ninety-nine patients were given either a placebo or 25 mg or 50 mg TVB-2640, orally, once-daily for 12 weeks. The study's primary endpoints were safety and the change in relative liver fat following therapy.

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Figure 3: Pharmacokinetic and pharmacodynamic assessments. (A) Plasma pharmacokinetic profile of TVB-2640 in 25-mg and 50-mg cohorts. (B) Tripalmitin, pharmacodynamic marker of FASN inhibition.

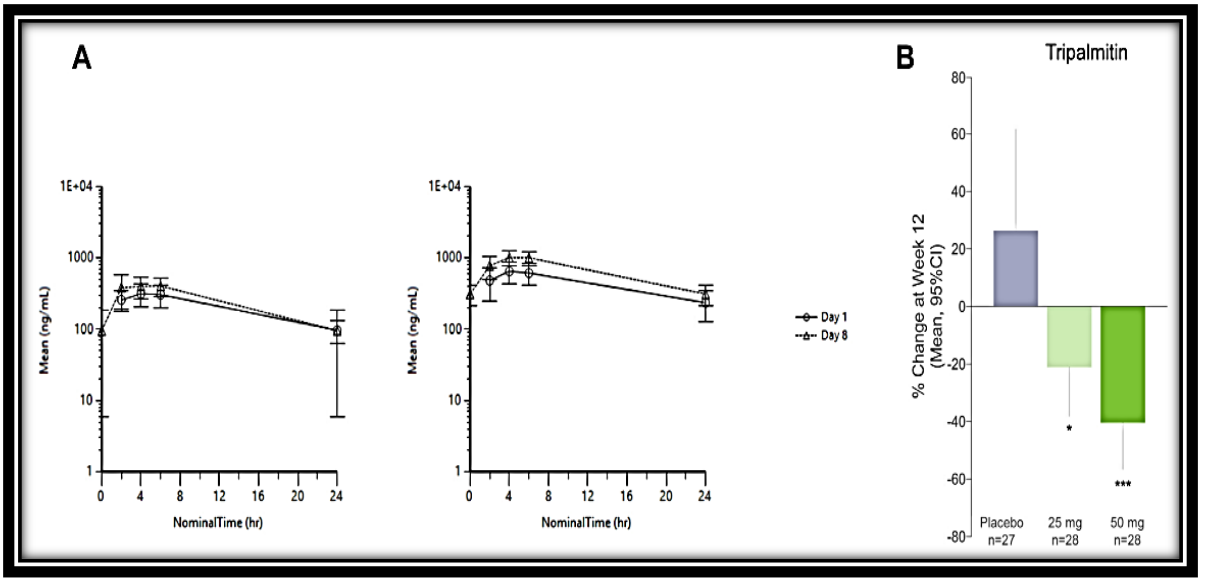
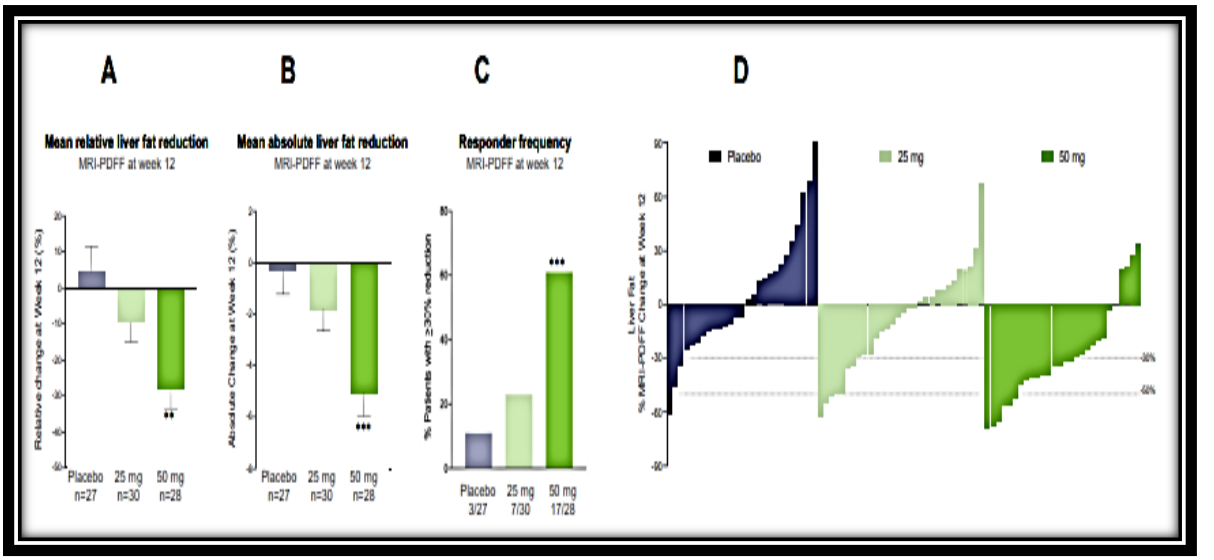


Figure 4: Changes in liver fat content measured by MRI-PDFF. (A) Relative change (percent change) of liver fat at week 12 relative to baseline (mean/standard error of mean [SEM]). (B) Absolute change of liver fat at week 12 relative to baseline (mean/ SEM). (C) Percent of patients with a > 30% relative decrease of liver fat. (D) Relative liver fat change at week 12 relative to baseline for each patient per treatment group.



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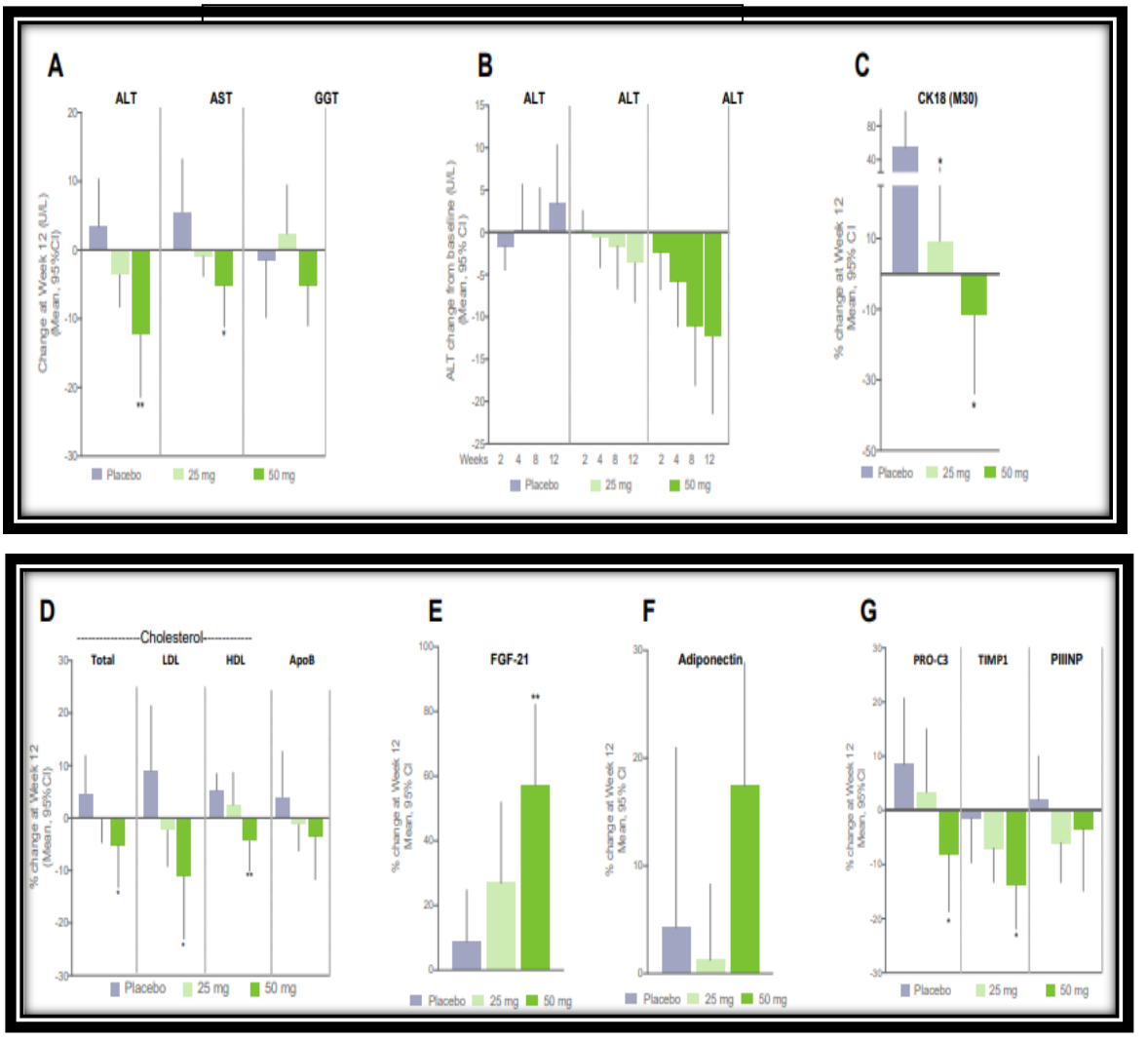
Results:

TVB-2640 reduced liver fat by 9.6% in the 25-mg cohort (n = 30; least squares mean: –15.5 percent; 95 percent confidence interval, –31.3 to –0.23; P = .053) and 28.1 percent in the 50-mg cohort (n = 28; least squares mean: –28.0 percent; 95 percent confidence interval, –44.5 to –11.6; P = 001). Patients in the placebo group had a >30% relative reduction in liver fat, compared to 23% in the 25-mg group and 61% in the 50-mg group (P < .001). Metabolic, pro-inflammatory, and fibrotic indicators all improved in secondary studies. TVB-2640 was well accepted, with most adverse events being modest and evenly distributed among the groups.



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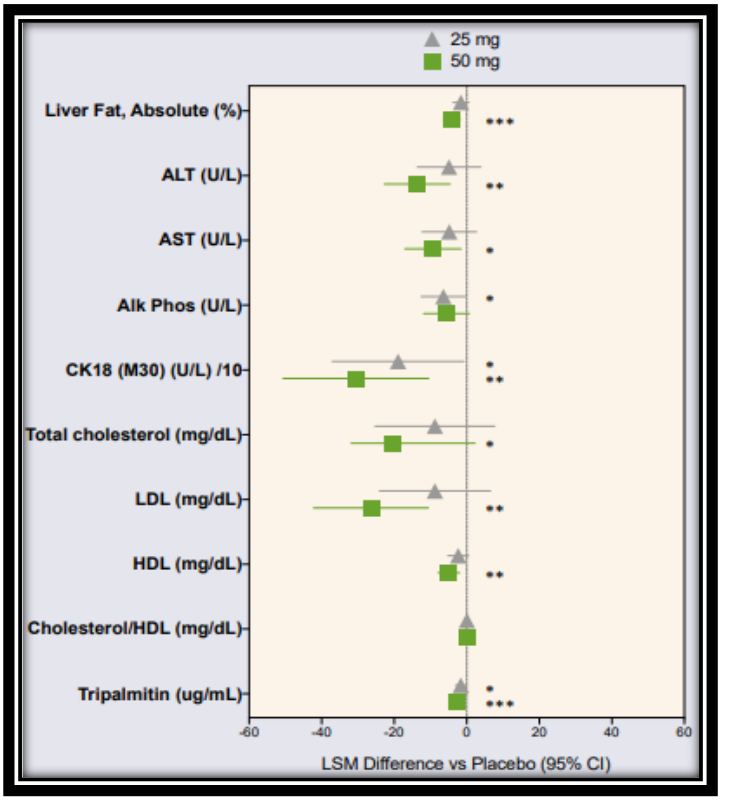

Figure 6: . Summary of effect of TVB-2640 on tripalmitin, liver injury markers and cholesterol profiles.

Conclusion:

After 12 weeks, TVB-2640 reduced liver fat and improved biochemical, inflammatory, and fibrotic indicators in individuals with non-alcoholic steatohepatitis in a dose-dependent manner.

Reference:

Loomba R, et al. TVB-2640 (FASN Inhibitor) for the Treatment of Nonalcoholic Steatohepatitis: FASCINATE-1, a Randomized, Placebo-Controlled Phase 2a Trial. Gastroenterology. 2021 Nov;161(5):1475-1486.

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