

IN BRIEF

COVID-19

Antibody responses to SARS-CoV-2 infection are attenuated in infliximab-treated patients with IBD

In patients with inflammatory bowel disease (IBD), use of the anti-TNF agent infliximab has been associated with reduced serological responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. 6,935 patients with IBD were recruited from 92 hospitals across the UK in the CLARITY study, and antibody responses to SARS-CoV-2 infection were examined in patients treated with infliximab or vedolizumab (a reference cohort). Rates of symptomatic and proven SARS-CoV-2 infection were similar between the groups, but seroprevalence was lower in the infliximab group than in the vedolizumab group (3.4% versus 6.0%, $P < 0.0001$). Seroconversion and the magnitude of anti-SARS-CoV-2 reactivity were also attenuated in the infliximab group. Moreover, serological responses in infliximab-treated patients were further diminished by concomitant immunosuppressor use (thiopurines or methotrexate; only 37% of these individuals had detectable SARS-CoV-2 antibodies); both infliximab and immunosuppressor use were independently associated with lower seropositivity.

ORIGINAL ARTICLE Kennedy, N. A. et al. Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab. *Gut* <https://doi.org/10.1136/gutjnl-2021-324388> (2021)

NAFLD

Examining the prevalence of NAFLD and NASH in a US cohort

The prevalence and severity of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) have been prospectively assessed in a large, middle-aged US cohort of asymptomatic individuals. MRI-based liver imaging alongside liver elastography was used to screen for NAFLD, and participants with abnormal imaging parameters were referred for liver biopsy to evaluate NASH. Of 835 participants, 664 met the inclusion and exclusion criteria: 50% were male, 52% had obesity and mean age was 56 ± 6.4 years. The prevalence of NAFLD and NASH was 38% (95% CI 34–41%) and 14% (95% CI 12–17%), respectively. Multivariable analysis revealed that factors associated with the presence of NASH included ethnicity, obesity and type 2 diabetes mellitus.

ORIGINAL ARTICLE Harrison, S. A. et al. Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. *J. Hepatol.* <https://doi.org/10.1016/j.jhep.2021.02.034> (2021)

COLORECTAL CANCER

Sugar intake during adolescence and risk of colorectal polyps

A new study examines the link between intake of simple sugar (fructose, glucose, added sugar and total sugar) and sugar-sweetened beverages (SSBs) in adolescence and risk of colorectal cancer (CRC) precursors. Data on dietary information and endoscopy results were analysed from 33,106 female participants of the Nurses' Health Study II. During follow-up, 2,909 conventional adenomas and 2,355 serrated lesions were identified (mean age at diagnosis 52.2 ± 4.3 years). High sugar and SSB intake during adolescence was positively associated with increased risk of colorectal adenoma (particularly rectal adenoma), but not serrated lesions. Notably, sugar and SSB intake during adulthood was not associated with risk of colorectal adenoma.

ORIGINAL ARTICLE Joh, H.-K. et al. Simple sugar and sugar-sweetened beverage intake during adolescence and risk of colorectal cancer precursors. *Gastroenterology* <https://doi.org/10.1053/j.gastro.2021.03.028> (2021)

THERAPY

Searching for therapies for advanced cirrhosis

Two new multicentre, randomized clinical trials report mixed results for the management of decompensated cirrhosis, showing no benefit of daily albumin infusions in this setting (ATTIRE trial) but that terlipressin was efficacious for the treatment of type 1 hepatorenal syndrome (HRS; CONFIRM study). Both trials reported potentially concerning serious adverse events, particularly related to pulmonary complications.

In the open-label, parallel-group ATTIRE trial, 777 hospitalized patients with decompensated cirrhosis (the majority owing to alcohol) and serum albumin levels < 30 g/l were randomly assigned to receive either targeted 20% human albumin solution daily for up to 14 days or until discharge to increase serum albumin levels to > 30 g/l ($n = 380$), or standard care in the UK (albumin infusions for draining ascites or renal failure; $n = 397$). The composite primary end point was new infection, kidney dysfunction or death between days 3 and 15 after treatment initiation.

Crucially, there was no statistically significant difference between the percentage of patients with a primary end point event in the targeted albumin group and the standard care group (29.7% versus 30.2%). Furthermore, more severe or life-threatening serious adverse events (including pulmonary oedema) occurred in the albumin group than the standard care group.

"Prior to ATTIRE, it was widely believed that albumin was the most appropriate fluid for resuscitation in hospitalized cirrhosis patients," explain authors Louise China and Alastair O'Brien. "These data strongly support both the need to abandon the use of this costly therapy, and a reappraisal of our understanding of this complex condition," they add, noting that the high mortality associated with cirrhosis has changed little over the years and calling for renewed focus on preventing the major causes

of liver disease, excessive alcohol consumption and obesity.

In the phase 3 CONFIRM trial, 300 patients with cirrhosis and type 1 HRS were randomly assigned in a 2:1 ratio to receive terlipressin (a vasoconstrictor; $n = 199$) or placebo ($n = 101$) for up to 14 days, with concomitant use of albumin strongly recommended in both groups. The primary end point was verified reversal of HRS. "Terlipressin, despite being a very old drug, is not approved in North America for any indication whatsoever," points out author Florence Wong. "This was the largest randomized controlled trial on the use of terlipressin for the treatment of type 1 HRS."

Importantly, terlipressin was more efficacious than placebo in improving renal function; verified HRS reversal was reported in 32% of the terlipressin group versus 17% in the placebo group ($P = 0.006$). However, more adverse events (abdominal pain, nausea, diarrhoea or respiratory failure) were reported with terlipressin than placebo. There was no difference in either overall or transplant-free survival, but a higher percentage of patients receiving terlipressin (22 patients, 11%) died within 90 days due to respiratory disorders than those receiving placebo (two patients, 2%).

"We clearly need to identify a group of patients with cirrhosis and renal dysfunction who would benefit the most from terlipressin," notes Wong. "One of the options is to treat patients at a lower level of serum creatinine, say stage 2 acute kidney injury rather than waiting for a fixed threshold of serum creatinine [level] of 2.5 mg/dL to be reached before starting treatment."

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ORIGINAL ARTICLES China, L. et al. A randomized trial of albumin infusions in hospitalized patients with cirrhosis. *N. Engl. J. Med.* **384**, 808–817 (2021) | Wong, F. et al. Terlipressin plus albumin for the treatment of type 1 hepatorenal syndrome. *N. Engl. J. Med.* **384**, 818–828 (2021)