The Effects of Immunotherapy on Current or Past HBV Infection

To evaluate the incidence of hepatitis flare, HBV reactivation, hepatitis B surface antigen (HBsAg) seroclearance or seroreversion in patients with current or past HBV infection who had received immunotherapy, evaluation was carried out. Immunotherapy had dramatically improved the survival of patients with advanced or metastatic malignancies, indicating this evaluation.

A territory-wide, observational cohort study was carried out in Hong Kong. Patients were identified through electronic medical records, based on the prescriptions of immune checkpoint inhibitors from July 1, 2014 to December 31, 2019. Patients who were HBsAg-positive or HBsAg-negative with results for antibody to hepatitis B surface or core antigen (anti-HBs or anti-HBc), were included.

A total of 990 patients (397 HBsAg-positive, 593 HBsAg-negative), with 482 anti-HBc and/or anti-HBs positive and 111 both anti-HBC and anti-HBs negative) were identified. All of HBsAg-positive and 15.9% HBsAg-negative were put on oral antiviral treatment. Hepatitis flare (ALT greater than 2 times the upper limits of normal), occurred in 39.3% HBsAg-positive and 30.4% HBsAg-negative patients. High baseline ALT and combination of immunotherapy increased the risk of hepatitis. HBV reactivation (greater than 2 logs increase in HBV DNA from baseline), occurred in 2 HBsAg-positive patients. HBsAg seroclearance and seroreversion was observed in 1 HBsAg-positive and 1 HBsAg-negative patient, respectively (less than 1%).

It was concluded that hepatitis flare occurs in possibly 40% of HBsAg-positive patients and 30% of HBsAg-negative patients during immunotherapy. HBV reactivation, HBsAg seroclearance and HBsAg seroconversion are rare. It was also concluded that current or past HBV infection has no impact on the emergence of hepatitis flare associated with immunotherapy.

Wong, G., Wong, V., Wing, V., et al. "Hepatitis Flare During Immunotherapy in Patients with Current or Past Hepatitis B Virus Infection." American Journal of Gastroenterology 2021; Vol. 116, pp. 1274-1283.

Aspirin and SSRI as Chemoprotection for Colorectal Cancer

To explore whether the use of aspirin and SSRI, either as monotherapy or combined, can have a clinical benefit against colorectal cancer (CRC), the development of CRC involves multiple dysfunctional pathways. A nested-case control study using nationwide Swedish registers was carried out, recruiting 24,786 CRC cases and randomly matched to 74,358 controls, conditional on birth year and sex using incidence density sampling.

Odds ratios were calculated from the conditional logistic regression model. Additive interaction was calculated as a relative excess risk for interaction and multiplicative interaction was calculated by including a product term in the regression model.

Both aspirin and SSRIs monotherapy were negatively associated with CRC risk, but the combined use of both was associated with even lower CRC risk (OR 0.77), than aspirin monotherapy (adjusted OR 0.91), and SSRI monotherapy adjusted (OR 0.93).

A significant interaction was observed at the additive scale with a relative excess risk for the interaction of -0.07, whereas no interaction was noted on the interactive scale. The inverse associations of CRC with aspirin and SSRIs showed a dose-dependent pattern.

It was concluded that the study suggested that the use of aspirin and SSRIs, either as monotherapy or combined, was associated with a reduced risk of CRC, but requiring further studies to confirm underlying mechanisms and allowing plausibility of clinical recommendation.

Zhang, N., Sundquist, J., Sundquist, K., et al. "Combined Use of Aspirin and Selective Serotonin Reuptake Indicators is Associated with Lower Risk of Colorectal Cancer: A Nested Case-Control Study." American Journal of Gastroenterology, 2021; Vol. 116, pp. 1313-1321.

Natural Treatment for Chronic Constipation in United States Patients

A partially randomized, comparative effectiveness trial was carried out, evaluating kiwi fruit, psyllium, and prunes in U.S. patients with CC. Randomization

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was carried out to 3 natural treatments and eligible patients had less than 3 complete spontaneous bowel movements (CSBMs) per week and were randomized to green kiwi fruit (2 per day), prunes (100 grams per day), or psyllium (12 grams per day), for 4 weeks. The primary endpoint was the proportion of patients in each group reporting an increase of greater than 1 CSBM per week, compared with baseline for at least 2 of 4 treatment weeks.

Key secondary outlines included stool frequency, stool consistency and straining assessed daily. Treatment satisfaction and adverse events (AEs) were also measured. Standard statistical measures were used.

A total of 79 patients with CC (mean age 42.7 years, 87% female and 77% white), were partially randomized. Complete data were available for 75 patients. For the primary endpoint, proportions of CSBM responders were similar for the treatments. For secondary outcomes, comparing treatment weeks 3 and 4 to baseline, there was a significant increase in weekly CSBM rate with all 3 treatments. Stool consistency significantly improved with kiwifruit and prunes and straining significantly improved with kiwifruit, prunes and psyllium. Patients randomized to the kiwi fruit group reported significant improvement in bloating scores. AEs were most common with psyllium and least common with kiwi fruit.

At the end of treatment, a smaller proportion of patients were dissatisfied with kiwifruit, compared with prunes or psyllium.

It was concluded that all 3 improved constipation symptoms in patients with CC, but kiwifruit was associated with the lowest rate of AEs and the lowest rate of dissatisfaction with therapy.

Chey, S., Chey, W., Jackson, K., Eswaran, S. "Exploratory Comparative Effectiveness Trial of Green Kiwifruit, Psyllium, or Prunes in U.S. Patients with Chronic Constipation." American Journal of Gastroenterology, 2021; Vol. 116, pp. 1304-1312.

Tenapanor Results in Treatment of IBS with Constipation

A phase-3 trial assessed the long-term efficacy and safety of tenapanor 50 mg b.i.d. for the treatment of patients with IBS with constipation (IBS-C). This drug is the first in class, minimally absorbed, small molecule inhibitor of the gastrointestinal sodium/hydrogen exchanger isoform-3.

In this randomized, double-blind study, patients with IBS-C received tenapanor 50 mg b.i.d. or placebo b.i.d. for 26 weeks.The primary endpoint was the proportion of patients who had a reduction of greater than 30% in average weekly worst abdominal pain and an increase greater than 1 weekly complete spontaneous bowel movement from baseline, both in the same week for greater than 6 of the first 12 treatment weeks (6/12 week combined responder).

A total of 620 randomized patients were included with IBS-C; 593 were included in the intention-to-treat analysis set (N = 293), placebo (N = 300), and 481 patients completed the 26-week treatment period. In the intention-to-treat analysis set, a significantly greater proportion of patients treated with tenapanor were 6/12 week combined responders than those treated with placebo (36.5% vs. 23.7%). Abdominal symptoms and global symptoms of IBS were significantly improved with tenapanor, compared with placebo.

Diarrhea, the most common adverse event (AE), was typically transient and mild to moderate in severity. Diarrhea led to study drug discontinuation for 19 (6.5%) and 2 patients receiving tenapanor and placebo, respectively.

It was concluded that tenapanor 50 mg b.i.d. improved IBS-C symptoms over 26 weeks and was generally well tolerated, offering a potential new long-term treatment option for patients with IBS-C.

Chey, W., Lembo, A., Yang, Y., Rosenbaum, D. "Efficacy of Tenapanor in Treating Patients with Irritable Bowel Syndrome with Constipation: A 26-Week, Placebo-Controlled, Phase-3 Trial (T3MPO-2). American Journal of Gastroenterology, 2021; Vol. 116, pp. 1294-1303.

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