Red Meat Consumption and Risk of Non-Alcoholic Fatty Liver Disease

To evaluate the association between meat consumption and risk of NAFLD in the Golestan Cohort Study (GCS), 50,045 participants were enrolled, age 40 to 75 years in Iran. Dietary information was collected using a 116-item, semi-quantitative food frequency questionnaire at baseline (2004 to 2008). A random sample of 1612 cohort members participated in a liver-focused study in 2011. NAFLD was ascertained through ultrasound.

Total red meat consumption and total white meat consumption were categorized into quartiles, based on the CGS population, with the first quartile as the reference group. Multivariable logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CI).

The median intake of total red meat was 17 grams per day and total white meat was 53 grams per day. During follow-up, 505 individuals (37.7%) were diagnosed with NAFLD and 124 of them (9.2%), had elevated ALT. High total red meat consumption (OR = 1.59) and organ meat consumption (OR = 1.70) were associated with NAFLD. Total white meat, chicken or fish consumption did not show significant association with NAFLD.

Hashimean, M., Merat, S., Poustchi, H., et al. "Red Meat Consumption and Risk of Non-Alcoholic Fatty Liver Disease in a Population With Low Meat Consumption: The Golestan Cohort Study." American Journal of Gastroenterology; Vol. 116, August 2021; pp. 1657 – 1675.

Updated Evaluation of Tegaserod for IBS-C

An integrated analysis on patient-reported outcomes relevant to current practice in the use of Tegaserod in IBS-C was carried out using data from four 12-week, randomized, placebo-controlled trials, evaluating that medication at 6 mg b.i.d. in patients with IBS-C. Two groups were analyzed. All were women younger than 65 years, without a history of cardiovascular ischemic events. The primary end point was subjective global assessment of IBS-C symptom relief. Responders rated themselves "considerably," or "completely relieved" greater than 50% of the time, or at least "somewhat relieved" 100% of the time over the last 4 weeks.

The population included 2,939 (Tegaserod 1,478; placebo 1,461) and 2,752 (Tegaserod 1,386; placebo 1,366) participants, respectively. The pooled odds ratios for clinical response during the last four weeks of the overall and indicated populations, clinical response rate for Tegaserod during the last four weeks were 43.3% and 44.1% vs. 35.9% and 36.5% with placebo. Adverse events were similar between groups. No significant cardiovascular event related to Tegaserod was observed in patients with one or less than one cardiac risk factor.

It was concluded that Tegaserod 6 mg b.i.d. reduced IBS-C symptoms in overall and US Food and Drug Administration indicated populations, including women aged less than 65 years with no history of cardiovascular ischemic events.

Shah, E., Lacy, B., Chey, W., et al. "Tegaserod for Irritable Bowel Syndrome with Constipation in Women Younger than 65 Years without Cardiovascular Disease: Pooled Analyses of 4 Controlled Trials." American Journal of Gastroenterology; Vol. 116, August 2021, pp. 1601-1611.

Steatosis and Steatohepatitis Effects on Patients with Chronic Hepatitis B

To investigate the impact of fatty liver disease (FLD) on liver disease severity in a large North American cohort with chronic hepatitis B viral infection, liver biopsies from 420 hepatitis B surface antigen-positive adults that were enrolled in the Hepatitis B Research Network and who were not on HBV therapy in the previous month were evaluated for inflammation and fibrosis. Steatohepatitis was based on steatosis, hepatocyte ballooning, with or without Mallory-Denk bodies and perisinusoidal fibrosis. The models evaluated factors associated with steatohepatitis, and the association of steatohepatitis with fibrosis and longitudinal ALT, AST, and Fibrosis-4.

The median age was 42 years and 62.5% were male, 79.5% were Asian. A total of 132 (31.4%) patients had FLD (77 - 18.3%), steatosis only, 55 – 13.1% had steatohepatitis. Older age, overweight/obesity and diabetes were associated

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with steatohepatitis. Steatohepatitis versus no FLD was associated with 1.6% times higher risk of advanced fibrosis at baseline and there was indication of higher incident cirrhosis rate during followup. Steatohepatitis versus no FLD was also independently associated with 1.39 times higher ALT, 1.25 times higher Fibrosis-4.

It was concluded that coexisting steatosis occurred in nearly one-third of adults of which 13% had steatohepatitis with chronic hepatitis B viral infection in this North American cohort who underwent liver biopsies. Steatohepatitis was associated with advanced fibrosis and higher biochemical measures of hepatic inflammation over time. There is indication for screening for and managing metabolic abnormalities in patients with HBV to prevent disease progression in HBV.

Khalili, M., Kleiner, D., King, W., et al. for the Hepatitis B Research Network (HBRN). "Hepatic Steatosis and Steatohepatitis in a Large North American Cohort of Adults with Chronic Hepatitis B." American Journal of Gastroenterology; Vol. 116, August 2021, pp. 1686-1697.

Ranitidine and Bladder Cancer

With knowledge that the carcinogen N-nitrosodimethylamine and increased urinary content of that component in humans, utilizing that drug to investigate whether ranitidine use is associated with increased bladder cancer risk, a nested, case-control study was conducted within the Primary Care Clinical Informatics Unit Research database, containing general practice records from Scotland. Bladder cancer cases, diagnosed between 1999 and 2011 were identified and matched with up to 5 controls, based on age, sex, general practice and date of registration.

Ranitidine, other H2 receptor agonists and proton pump inhibitors were identified from prescribing records. Odds ratios (ORs) and 95% confidence intervals were calculated using conditional logistic regression after adjusting for comorbidities and smoking.

A total of 3260 cases were reviewed with 14,037 controls. There was evidence of increased risk of bladder cancer in ranitidine users, compared with nonusers (OR = 1.22), which was more marked with use over 3 years of ranitidine therapy (OR = 1.43). By contrast, there was little evidence of any association between PPI use and bladder cancer risk, based on any use (OR = 0.98), or over 3 years of use (OR = 0.98).

In this large population-based study, the use of ranitidine, particularly long-term, was associated with an increased risk of bladder cancer.

Cardwell, C., McDowell, R., Hughes, C., et al. "Exposure to Ranitidine and Risk of Bladder Cancer: A Nested, Case-Control Study." American Journal of Gastroenterology; Vol. 116, August 2021, pp. 1612-1619.

Colorectal Cancer in 18- to 49-Year-Olds

To evaluate CRC detection rates in a large, integrated healthcare system to assess treatment outcomes in younger CRC patients and to determine factors that could aid in identifying these individuals, confirmed cases of CRC were analyzed using a cancer database spanning from 1985 to 2017, from a large, integrated healthcare system composed of 15 hospitals, 150 outpatient clinics and 20 outpatient oncology clinics. Three cohorts were evaluated (18-44 years, 45-49 years and greater than 50 years).

Significant increases in CRC detection were seen in the cohort aged 18-44 (annual change 2.7%), and the cohort age 45-49 (annual percentage change 4.15%). The higher proportion of African-Americans, Hispanic and obese subjects were seen in the younger cohorts. A family history of CRC was found in 49% of the patients aged 18-44 and 38% of patients aged 45-50. Patients younger than age 50 were more likely to have metastases at diagnosis (6.8%) vs. the cohort over 50 (4.15%).

Survival was better in younger cohorts and they were more likely to receive multimodality treatment (surgery with chemotherapy or radiation). Survival probability was similar in different ethnic groups.

It was concluded that CRC is increasing at similar rates in young people aged 18-44 and 45-49, and that they are more likely to present with advanced disease needing multimodality treatment. A family history identifies some patients less than 50 years of age. Young patients presented with changes in bowel habit, rectal bleeding, anemia,

and weight loss should include colonoscopy in evaluation. Rectal and anal symptoms should prompt careful physical and endoscopic evaluation.

Vakil, N., Ciezki, K., Singh, M. "Colorectal Cancer in 18- to 49-year-olds: Rising Rates, Presentation, and Outcome in a Large Integrated Health System." Gastrointestinal Endoscopy; Vol. 94, No. 3, 2021; pp. 618-626.

USDA Efficacy in PBC with Compensated Cirrhosis

A retrospective cohort study of veterans, predominantly men with PBC and compensated cirrhosis were evaluated to assess the association of response to UDCA with the development of all-cause and liver-related mortality for transplantation, hepatic decompensation, and HCC-using, competing risk time-updating Cox proportional hazards models.

A total of 501 subjects with PBC and compensated cirrhosis, including 287 UDCA responders, (1692.8 patient-years {PY} of follow-up) and 214 partial responders (838.9 PY of follow-up). The unadjusted rates of hepatic decompensation (3.8 vs 7.9 per 100 PY), and liver-related death or transplantation (3.7 vs 6.2 per PY), were lower in UDCA responders compared with partial responders. UDCA response was associated with a lower risk of hepatic decompensation (subhazard ratio {sHR} 0.54), death from any cause or transplantation (aHR 0.49), and liver-related death or transplantation (sHR 0.40), but not HCC (sHR 0.39). In a sensitivity analysis, the presence of portal hypertension was associated with the highest UDCA-associated effect.

It was concluded that UDCA response is associated with a reduction in decompensation, all-cause, and liver-related death or transplantation in a cohort of predominantly male patients with cirrhosis, with the highest benefit in patients with portal hypertension.

John, B., Khakoo, N., Schwartz, K., et al. "Ursodeoxycholic Acid Response is Associated with Reduced Mortality in Primary Biliary Cholangitis with Compensated Cirrhosis." American Journal of Gastroenterology; Vol. 116, September 2021, pp. 1913-1923.

High SVR in Treatment of HCV with Suboptimal Dosing Adherence

The impact of efficacy for treatment with direct-acting antiviral drugs in the treatment of HCV infection with suboptimal adherence, particularly with shorter treatment durations was evaluated further. Evaluation with post-hoc analyses evaluated adherence (based on pill count), in patients prescribed 8- or 12- week Glecaprevir/Pibrentasvir (G/P), the impact of nonadherence on the SVR at post-treatment week 12 (SVR12), and the factors associated with nonadherence and efficacy in patients interrupting G/P treatment.

Data was pooled from 10 phase 3 clinical trials of treatment-naïve patients with HCV genotype 1-6, without cirrhosis, with compensated cirrhosis (treatment adherence analysis), and 13 phase 3 clinical trials of all patients with HCV (interruption analysis).

A total of 2,149 patients were included. Overall meet adherence was 99.4%. Over the treatment duration, adherence decreased (week 0-4 – 100%; weeks 5-8 – 98.3%, and weeks 9-12; 97.1%). The percentage of patients with greater than 80% or 90% adherence declined. SVR12 rate in the intention-to-treat (ITT) population was 97.7% and remained high in nonadherent patients in a modified ITT population.

Psychiatric disorders were associated with less than 80% adherence and shorter treatment duration was associated with greater than 80% adherence. Among 2,902 patients in the interruption analysis, 33 (1.1%) had a G/P treatment interruption of greater than 1 day with an SVR12 rate of 93.9% (31/33). No virologic failures occurred.

The findings support the impact of treatment duration and adherence rate and further reinforce the concept of "treatment forgiveness" with direct-acting antivirals.

Zamor, P., Brown, A., Dylla, D., et al. "High-Sustained Virologic Response Rates of Glecaprevir/Pibrentasvir in Patients with Dosing Interruption or Suboptimal Adherence." American Journal of Gastroenterology; Vol. 116, September 2021, pp. 1897-1904.

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