8 • INTESTINAL DISORDERS
FDA approves subcutaneous vedolizumab for Crohn's.

11 • CLINICAL PRACTICE UPDATE
AGA defines best approach to cannabinoid hyperemesis syndrome.

18 • UPPER GI TRACT
How dupilumab is improving treatment for eosinophilic esophagitis.

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GI&Hepatology News

June 2024

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AGA

Arithmedics, which uses AI technology to automate billing codes, won the Shark Tank competition at the 2024 AGA Tech Summit. Pictured are company founders Renumathy Dhanasekaran, MD, PhD, (left) and Venthan Elango, PhD.

Artificial Intelligence Wins AGA's Shark Tank Competition

BY JIM KLING

MDedge News

FROM THE 2024 AGA TECH SUMMIT

CHICAGO — At the 2024 AGA Tech Summit, held April 11-12 at the Chicago headquarters of MATTER, a global healthcare startup incubator, five companies made their pitch to be the winner of the Shark Tank competition that recognizes an outstanding tech start up in the gastroenterology field.

After the companies' rapid-fire pitches and Q&A sessions, four judges convened to determine a winner and returned to make an announcement.

The winner was Arithmedics, which uses AI technology to automate billing codes. Founder Venthan Elango, PhD, has worked as a software engineer at Google, Urban Engines, and Georgia Tech, and his wife of 17 years is Renumathy Dhanasekaran, MD, PhD, a gastroenterologist

See **Shark Tank** · *page 21*

Member **SPOTLIGHT**

Minnesota GI Talks 'Therapeutic Diets'

Wins Distinguished Clinician Award

BY JENNIFER LUBELL

What exactly is a healthy diet?

Scott Ketover, MD, AGAF, FASGE, will be the first to admit that's not an easy question to answer. "As much research and information as we have, we don't really know what a healthy diet is," said Dr. Ketover, president and CEO of MNGI Digestive Health in Minneapolis, Minnesota. He was recognized by AGA this year with the Distinguished Clinician Award in Private Practice.

When patients ask questions about a healthy diet, Dr. Ketover responds with a dose of common sense: "If it's food that didn't exist in the year 1900, don't eat it." Your grandmother's apple pie is fine in moderation, he notes but the apple pie you get at the fast food drive-through could sit on your shelf for 6 months and look the same.

That is not something you should eat, he emphasizes.

"I really do believe though, that what crosses our lips and gets into our GI tract really underlies our entire health. It's just that we don't have enough information yet to know how we can coach people in telling them: eat this, not that," Dr. Ketover added.

In an interview with *GI & Hepatology News*, Dr. Ketover spoke more about the link between the gut microbiome and overall health, and the young patient who inspired him to specialize in gastroenterology.

See **Wellness** · *page 22*

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LETTER FROM THE EDITOR

Celebrating Excellence

As we settle back into our daily routines following another fantastic DDW, I'd like to take a moment to congratulate this year's AGA's Recognition Award recipients, who have made outstanding contributions to the organization and to our field, including through excellence in clinical practice, research, mentorship, and DEI.

Dr. Adams

I'd like to… congratulate this year's AGA's Recognition Award recipients, who have made outstanding contributions to the organization.

This month's Member Spotlight column highlights one of these remarkable individuals, Dr. Scott Ketover, president and CEO of MNGI Digestive Health, who is the recipient of this year's AGA Distinguished Clinician Award in Private Practice. We hope you enjoy learning more about Scott, as well as the other award recipients who were recognized at a special ceremony in DC last month.

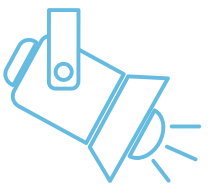
Also highlighted in our June issue is the FDA's recent approval of subcutaneous vedolizumab for Crohn's maintenance therapy, an exciting development that will provide us with more flexible treatment options for our patients. We also report on the 2024 AGA Tech Summit (Chicago, IL), and introduce the winners (survivors?) of its annual Shark Tank competition, Dr. Renu Dhanasekaran and Dr. Venthan Elango. Their company, Arithmedics, which developed technology that harnesses generative AI and data intelligence to streamline medical billing, was identified as the most promising among a robust field of entrants.

We also present some of the best clinically oriented content from our GI journals, including an observational study from *Gastroenterology* evaluating the effect of longitudinal alcohol use on risk of cirrhosis among patients with steatotic liver disease, and summarize recently released AGA Clinical Practice Updates on performance of high-quality upper endoscopy and treatment of cannabinoid hyperemesis syndrome. We hope you enjoy all the exciting content featured in this issue and take some well-deserved time to rest and recharge this summer!

Megan A. Adams, MD, JD, MSc
Editor in Chief

Maskot/Getty Images

Call for Nominations



Member SPOTLIGHT

Nominate your colleagues to be featured in Member Spotlight. Email GIHepNews@gastro.org.

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Linaclotide Proves Successful in Treating Functional Constipation in Children

BY HEIDI SPLETE

Children and adolescents with functional constipation showed significantly greater increases in spontaneous bowel movements with linaclotide compared with placebo, according to data from 330 individuals.

"Functional constipation is prevalent in pediatrics and is associated with chronic burdensome symptoms and impaired quality of life with an unmet need for treatment options for this age group," corresponding study author Julie Khlevner, MD, AGAF, a pediatric gastroenterologist at Columbia University Vagelos College of Physicians and Surgeons, New York, said in an interview.

Dr. Khlevner

"Linaclotide has been approved for adults with chronic idiopathic constipation and irritable bowel syndrome with constipation, but its efficacy and safety in pediatric patients were unknown. Therefore, evaluating its use in this population was crucial to provide evidence-based treatment option," she said.

In a study published in *The Lancet Gastroenterology & Hepatology* (2024 Jan 8. doi: 10.1016/S2468-1253(23)00398-9), the researchers randomized 166 pediatric patients with functional constipation to 72 micrograms of linaclotide once daily for 12 weeks and 164 to a placebo. The study was conducted at 64 clinic or hospital sites across 7 countries between October 1, 2019, and March 21, 2022. Approximately half (55%) of the patients were female.

The primary outcome was a change from baseline to 12 weeks in the frequency of spontaneous bowel movements (SBMs) per week, with no rescue medication on the day of or before the bowel movement. The secondary endpoint was change in stool consistency from baseline to 12 weeks. The mean frequency for SBMs at baseline was 1.16 per week in patients randomized to linaclotide and 1.28 for those randomized to placebo; these rates increased to 3.41 and 2.29, respectively, over the study period. The linaclotide patients showed a significantly greater improvement over placebo patients based on least-squares mean change from baseline (2.22 vs. 1.05, $P = .0001$).

In a subgroup analysis by age, the response was stronger in younger patients aged 6-11 years than in those aged 12-17 years, the researchers noted. This difference might stem from different pathophysiological mechanisms between older and younger ages, such as withholding behavior, they added.

Linaclotide was well tolerated overall; the most frequently reported treatment-emergent events were diarrhea (seven linaclotide patients and three placebo patients). In addition, five linaclotide patients and four placebo patients developed COVID-19 during treatment. No deaths occurred during the study, but one serious adverse event involving severe diarrhea, dehydration, and hospitalization, occurred in a 17-year-old female patient, but resolved after administration of intravenous fluids, the researchers noted.

Clinical Implications and Next Steps

The study findings reflect previous research on linaclotide in adults, Dr. Khlevner said. "The significant improvement in spontaneous bowel movements frequency and stool consistency with linaclotide compared to placebo is consistent with its mechanism of action as a guanylate cyclase C agonist," she noted.

In clinical practice, barriers to the use of linaclotide may include lack of awareness of linaclotide's safety and efficacy profile, and of its Food and Drug Administration approval for use in children aged 6-17 years with functional constipation, said Dr. Khlevner. "Additionally, access to the medication and insurance coverage may be potential barriers for some patients." However, "some of these barriers can be overcome through education and training of healthcare providers regarding the appropriate use of linaclotide in pediatric patients with functional constipation," she added.

The findings were limited by several factors including potential measurement bias and selection bias, lack of assessment of lifestyle modifications as confounding factors, and lack of quality-of-life assessment, the researchers noted. Other limitations included the relatively short 12-week treatment duration, which may not fully capture long-term safety and efficacy, and the focus on patients aged 6-17 years, Dr. Khlevner told this news organization.

"Future research could address these limitations through longer-term studies with broader age ranges and incorporating patient-reported outcomes in real world situations to assess the overall impact of linaclotide treatment on pediatric patients with functional constipation," she said.

Study Supports Noninvasive Treatment Option

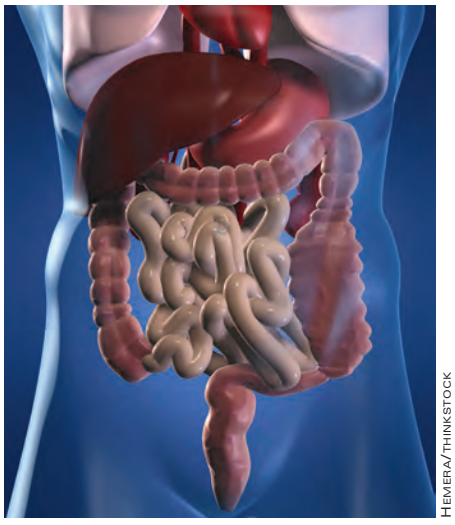
An alternative medication for children with functional constipation who do not respond to current therapies could prevent the use of more invasive interventions such as frequent enemas or antegrade enemas, Stephen M. Borowitz, MD, professor of pediatrics at the University of Virginia, Charlottesville, said in an interview.

Dr. Borowitz said he was not surprised by study findings. "Given the mechanism of action of the drug, I would expect the majority of children with functional constipation to respond in the sense of having more frequent and softer stools," he said. "The bigger question, which wasn't answered, is whether children who fail more conservative therapies respond to linaclotide," said Dr. Borowitz, who was not involved in the study. "This was a phase 3 trial of otherwise healthy children with functional constipation and we know the majority of these children will respond to aggressive management with osmotic stool softeners, plus or minus a stimulant like senna coupled with lifestyle modifications (such as drinking more fluid, regular toileting, and appropriate toileting behaviors)," he said.

The greatest short-term barrier to the expanded use of linaclotide in clinical practice will likely be cost, and whether insurance will cover the drug, Dr. Borowitz told this news organization. Insurance coverage may not be an option until the child has failed more conservative, less expensive therapies, he said.

Also, the current study was a placebo-controlled trial, and not a comparison between linaclotide and polyethylene glycol, plus or minus senna, with other routine interventions, he said.

Looking ahead, "now that we know linaclotide is better than placebo, we need to know if it is as good, better, or worse than other proven interventions, and perhaps even more importantly, is it effective among children who have failed more conservative management," Dr. Borowitz said. "We also need to know long-term risks, and given that the majority of childhood constipation develops before age 6 years, whether the drug can be used in younger children," he emphasized.



HEMERA/THINKSTOCK

If so, studies need to examine whether linaclotide alters the natural history of the problem, he added. Previous studies suggest that the longer the symptom goes on, the harder it is to undo the secondary behaviors that result, such as withholding, pelvic floor dysfunction, and toileting refusal, he noted.

The study was supported by AbbVie and Ironwood Pharmaceuticals. The lead author, Carlo Di Lorenzo, MD, disclosed consulting fees from AbbVie, Ironwood Pharmaceuticals, Mallinckrodt, NeurAxis, QOL Medical, and Takeda. Dr. Khlevner disclosed honoraria from Abbott Pediatric Nutrition and participation on a data safety monitoring board and advisory board for AbbVie. Dr. Borowitz had no financial conflicts to disclose. ■

FDA Gives Approval to Subcutaneous Vedolizumab for Crohn's Maintenance Therapy

BY MEGAN BROOKS

The US Food and Drug Administration (FDA) has approved the subcutaneous administration of vedolizumab (Entyvio) for maintenance therapy in adults with moderately to severely active Crohn's disease (CD) after induction therapy with intravenous (IV) vedolizumab.

The move follows the FDA's approval last year of subcutaneous vedolizumab for maintenance treatment of adults with moderately to severely active ulcerative colitis (UC).

The humanized immunoglobulin G1 monoclonal antibody is available as a single-dose prefilled pen (Entyvio Pen).

The FDA first approved the IV formulation of the biologic in 2014 for patients with moderate to severe UC and CD who cannot tolerate other therapies or in whom such therapies have failed.

The approval of subcutaneous vedolizumab for maintenance treatment of CD is based on the phase 3, randomized, double-blind, placebo-controlled VISIBLE 2 trial.

The trial enrolled 409 adult patients with moderately to severely active CD who had clinical response at week 6 following two doses of open-label IV vedolizumab at weeks 0 and 2.

Dr. Ritter

At week 6, they were randomly allocated in a 2:1 ratio to receive vedolizumab 108 mg administered by subcutaneous injection or placebo every 2 weeks. The primary endpoint was clinical remission at week 52, which was defined as a total Crohn's Disease Activity Index score ≤ 150.

The results showed that significantly more patients receiving subcutaneous vedolizumab than placebo achieved long-term clinical remission (48% vs 34%; $P < .01$), the company said in a news release.

The safety profile of subcutaneous vedolizumab is generally consistent with the known safety profile of IV vedolizumab, with the addition of injection-site reactions (including injection-site erythema, rash, pruritus, swelling, bruising, hematoma, pain, urticaria, and edema).

"Crohn's disease is a complex and usually progressive disease for which an appropriate management plan is critical. My primary goal as a clinician is always to get patients to achieve remission," Timothy Ritter, MD, senior medical director, GI Alliance Research, and assistant professor of medicine, Burnett School of Medicine at TCU, Fort Worth, Texas, said in the news release.

"In VISIBLE 2, about half of patients treated with Entyvio SC achieved long-term clinical remission. The data from VISIBLE 2 reaffirm the well-established efficacy profile of Entyvio, regardless of route of administration," Dr. Ritter added. ■

Liquid Biopsy Promising for Early Pancreatic Cancer Detection

BY M. ALEXANDER OTTO, PA, MMS

SAN DIEGO — A liquid biopsy assay that combines a microRNA signature and a well-known biomarker for pancreatic cancer has demonstrated an accuracy of 97% for detecting stage I/II pancreatic ductal adenocarcinoma, the most common type of pancreatic cancer.

[The investigators] developed a signature for pancreatic cancer based on microRNAs identified in the exomes shed from pancreatic cancers and cell-free DNA markers found in the blood of patients with the disease.

It is quite encouraging to know we have a blood test that could potentially find this disease early, said Ajay Goel, PhD, a molecular diagnostics specialist at City of Hope in Duarte, California, who presented the findings at the annual meeting of the American Association for Cancer Research (AACR).

Dr. Goel and colleagues developed a signature for pancreatic cancer based on microRNAs identified in the exomes shed from pancreatic cancers and cell-free DNA markers found in the blood of patients with the disease.

Their initial assay tested blood samples for this signature in a training cohort of 252 people in Japan, approximately 60% of whom had pancreatic cancer. The rest were healthy controls. The assay was then tested in validation cohorts of 400 subjects, half with pancreatic cancer and half controls, in China and South Korea.

In both the initial and validation tests, the microRNA assay had an accuracy of about 90% for stage I/II pancreatic cancer, already far better than commercially available assays.

In an additional validation cohort in the United States with 139 patients with pancreatic cancer and 193 controls at six centers across the country, the researchers found that adding carbohydrate antigen 19-9 — a well-known marker of pancreatic cancer — to the assay boosted the test's accuracy to 97%.

The test performed the same whether the tumor was in the head or tail of the pancreas.

"We are very excited about this data," said Dr. Goel.

The technology was recently licensed to Pharus Diagnostics for commercial development, which will likely include a prospective screening trial, he told this news organization.

Because pancreatic cancer is fairly uncommon, Dr. Goel did not anticipate the test being used for general screening but rather for screening high-risk patients such as those with newly diagnosed type 2 diabetes, a family history of pancreatic cancer, or predisposing genetic mutations.

Almost 4,000 subjects have been enrolled in ongoing validation efforts, and efforts are underway to use the test to screen thousands of banked blood samples from the PLCO, a prospective cancer screening trial in healthy subjects.

"It should be a very inexpensive test; it doesn't cost us much to do in the lab," he added.

Study moderator Ryan Corcoran, MD, PhD, a gastrointestinal (GI) oncologist at Massachusetts General Hospital, Boston, saw the potential.

"As a GI oncologist, I know how lethal and hard to treat pancreatic cancer is," he said. A test that could reliably detect pancreatic cancer early, with an acceptable false-positive rate, would be extremely useful.

"The cure rate is many, many times higher," if we detect it before it has a chance to spread, he explained.

In the meantime, Dr. Goel said there's more work to be done.

Almost 4,000 subjects have been enrolled in ongoing validation efforts, and efforts are underway to use the test to screen thousands of banked blood samples from the PLCO, a prospective cancer screening trial in healthy subjects.

The researchers also want to see if the test can distinguish benign pancreatic cysts from ones that turn cancerous.

The idea is to find the earliest possible signs of this disease to see if we can find it not "at the moment of clinical diagnosis, but possibly 6 months, 1 year, 2 years earlier" than with radiologic imaging, Dr. Goel said.

The work was funded by the National Cancer Institute and others. Dr. Goel is a consultant for Pharus Diagnostics and Cellomics. Dr. Corcoran is a consultant for, has grants from, and/or holds stock in numerous companies, including Pfizer, Novartis, Eli Lilly, and Revolution Medicines. ■

Genes May Govern Intestinal Sites of Pediatric Crohn's

BY DIANA SWIFT

FROM CELLULAR AND MOLECULAR GASTROENTEROLOGY AND HEPATOLOGY

Genetic predisposition likely directs intestinal disease location in pediatric Crohn's disease (CD) — whether colon-predominant (C-CD) or small-bowel-predominant (SB-CD), a small analysis in *Cellular and Molecular Gastroenterology and Hepatology* suggests (2024 Feb. doi: 10.1016/j.jcmgh.2024.02.010).

Richard Kellermayer, MD, PhD, of the Section of Pediatric Gastroenterology, Hepatology and Nutrition at Baylor College of Medicine in Houston, Texas, and colleagues compared the genetic makeup of patients based on their Crohn's disease location — predominantly in the small bowel (L4) or predominantly in the colon (L2 and/or L3). They then generated bipartite networks of susceptibility genes to study the polygenic background of the disease subtypes. They hypothesize that such networks may govern where a patient develops Crohn's disease.

According to current understanding, as Dr. Kellermayer told *GI & Hepatology News*, most autoimmune disorders, CD included, develop in people with a genetic predisposition after serial environmental insults between conception and young adulthood. "As opposed to single-gene-associated genetic disorders, autoimmune diseases are linked to several hundred genes in which subtle anomalies can work in concert to predispose someone to a certain disorder," he said. "We hope our findings will guide the development of personalized treatments based on the disease location at diagnosis to advance precision medicine."


Dr. Kellermayer

Eight cases of SB-CD and 11 of C-CD met the inclusion criteria. Mean age at CD diagnosis was about 11 years for both subtypes, while 36.3% of patients with C-CD were female vs 25% of those with SB-CD. Ethnicity was 72.2% White in the C-CD group and 87.5% in the SB-CD group.

As to the main ileocolonic locations according to the Paris Classification of pediatric inflammatory bowel disease, 54.5% in the C-CD group had involvement at L2 and 45.5% at L3. In SB-CD cases, 100% had disease at L4b, 37.5% at L4, and 50% at L1.

The researchers identified 115 single-nucleotide polymorphisms (SNPs) with a combined annotation-dependent depletion (CADD) score on Phil's Read Editor (PHRED) of >10 that was associated with 97 genes. PHRED is a computer program measuring the quality of the identification of nucleobases generated by automated DNA sequencing and scores the deleteriousness of single-nucleotide variants. The identified genes in this study had a significantly ($P < .01$) different allele variation between C-CD and SB-CD.

Among the top 28 candidates was an SNP in the *EFNA3* gene with a CADD score > 20 for differentiating between the two phenotypically distinct CD groups. Furthermore, the *EFNA3* rs17723260 (predicted to be deleterious) was found to have a significantly lower allele frequency (4.5%) in C-CD compared with its allele frequency of 37.5% in SB-CD (chi square $P = .0097$).

"This finding indicates that *EFNA3* might play a role in modulating colonic inflammation, in which a deleterious genetic defect might provide protection against colitis (and direct autoimmunity against the proximal small bowel) in the polygenic background of CD," the investigators wrote.

EFNA3 has been linked to both CD and ulcerative colitis. Another four genes associated with the top five SNP candidates had already been connected with IBD or mammalian intestinal inflammation.

According to the authors, the biomedical literature and mouse model findings "implicate the translational relevance of our candidate gene compendium for directing colon- vs small-bowel–predominant CD development." They hope the findings will be replicated in larger CD cohorts differentiated by disease location.

This study was supported by the ProKIIDS Network of the Crohn's and Colitis Foundation, the Public Health Service, the Wagner, Frugoni, and Klaasmeyer families' Gutsy Kids Fund, and by the DR and GL Laws Fund. The authors disclosed no conflicts of interest.

Real-World HDV Study Characterizes Responses to Bulevirtide

BY WILL PASS

FROM GASTRO HEP ADVANCES

Some hepatitis D virus (HDV)-infected patients may require longer treatment with bulevirtide than others, but even "nonresponders" according to US Food and Drug Administration (FDA) criteria may achieve reduced viremia with ALT normalization, based on real-world experience.


Dr. Killer

These findings suggest that longer follow-up is needed to determine the optimal treatment duration for bulevirtide monotherapy, reported lead author Alexander Killer, MD, of Heinrich Heine University Düsseldorf, Germany, and colleagues.

Bulevirtide was conditionally approved by the European Medicines Agency in 2020 and is on track for full marketing approval in Europe, but remains unavailable in the United States, where Gilead, the manufacturer, has faced regulatory hurdles.

In the MYR202 and 301 clinical trials, bulevirtide significantly reduced HDV-RNA levels in 54% of patients after 24 weeks, and reduced viremia while normalizing ALT in 48% of patients after 48 weeks.

"Given its standalone status and good treatment tolerance even in patients with compensated cirrhosis, this represents a step change in the treatment of HDV-coinfected individuals," Dr. Killer and colleagues wrote in *Gastro Hep Advances* (2024 Jan 5. doi: 10.1016/j.gastha.2024.01.001).

Yet dynamics of response and clinical predictors of treatment outcome remain unclear, prompting Dr. Killer and colleagues to conduct the present retrospective study. The dataset included 15 patients who received bulevirtide for at least 1 year at a single center in Germany.

The analysis focused on monthly changes in biochemical and virologic parameters. The investigators also screened for clinical factors that might predict responses to therapy.

Treatment response rate and safety profile aligned with data from clinical trials, suggesting that bulevirtide is safe and effective in a real-world setting.

Patients typically achieved ALT normalization 2-6 months into therapy, followed by virologic response at least 6 months after starting treatment, with one-third of patients requiring at least 1 year to achieve HDV-RNA negativity.

"Of note, normalization of ALT under bulevirtide treatment occurs earlier than the decline of HDV-RNA levels, which contrasts with the response seen to nucleos(t)ide analog treatment in hepatitis B," the investigators wrote. They suggested that this may be due to bulevirtide's distinct mechanism of action.

Severe hepatitis was associated with lower response rates in the first year. Possible predictors of delayed response included low body mass index and high alpha-fetoprotein.

Of note, two patients had ALT normalization without virologic response.

"It is unclear whether these patients actually have worse outcomes in terms of overall success than patients with a combined response, especially since these patients experienced a decline of more than 1 log," Dr. Killer and colleagues wrote, noting that a 1 log reduction is considered an intermediate virologic response, and hepatitis B virus (HBV) studies have shown that severe liver events are prevented by early ALT normalization. "Therefore, it does not seem appropriate to categorize patients with biochemical responses as 'treatment nonresponders'."

The investigators called for longer observational studies to determine the optimal duration of bulevirtide monotherapy.

This study was funded by the German Research Foundation. The investigators disclosed relationships with Novartis, GSK, AbbVie, and others.

High Alcohol Intake in MASLD Raises Cirrhosis Risk

BY DIANA SWIFT

FROM GASTROENTEROLOGY

One in nine patients with steatotic liver disease reported concurrent alcohol use, and more than 11% reported high-risk consumption, a national study of more than a million US veterans found.


Dr. Wong

Moreover, the combination of steatotic liver disease and high-risk alcohol intake carried a more than 43% higher long-term risk of liver cirrhosis compared with no alcohol use, according to researchers led by Robert J. Wong, MD, MS, of the Division of Gastroenterology and Hepatology, Veterans Affairs Healthcare System Palo Alto, at Stanford University School of Medicine in Palo Alto, California.

However, the study found that "reducing alcohol use lowers risk of cirrhosis, emphasizing the importance of timely alcohol use assessment and early interventions to address high-risk alcohol use in steatotic liver disease," Dr. Wong and associates wrote in *Gastroenterology* (2024 Feb 28. doi: 10.1053/j.gastro.2024.02.032).

Although concurrent moderate to heavy alcohol intake would be expected to lead more rapidly to liver disease progression, the existing literature has been conflicting, the authors noted. Several studies have even found moderate alcohol associated with a lower risk of advanced liver disease among MASLD patients, including that by Dunn et al. (J Hepatol. 2012 Apr 18. doi: 10.1016/j.jhep.2012.03.024).

MASLD patients were identified through the US Veterans Affairs Corporate Data Warehouse from January 1, 2010, through December 31, 2017, with follow-up through December 31, 2022.

Alcohol use was assessed by Alcohol Use Disorders Identification Test–Concise (AUDIT-C) scores and was categorized as follows: no alcohol (AUDIT-C = 0), low-risk alcohol use (AUDIT-C 1-2 for women and 1–3 for men), and high-risk alcohol (AUDIT-C ≥ 3 for women and ≥ 4 for men).

Among the 1,156,189 veterans with MASLD, 54.2% reported no alcohol, 34.6% low-risk alcohol, and 11.2% high-risk alcohol use. In median follow-up of nine to 10 years, incidence rates of cirrhosis were .53 per 100 person-years for no use, .42 for low-risk use, and .76 for high-risk use.

In contrast to patients with baseline high-risk alcohol intake who reported no change in use, those who decreased their alcohol intake during follow-up experienced a 39% reduction in the long-term risk of cirrhosis, for a hazard ratio of .61 (95% CI, .45-.83, $P < .01$).

About 70% of patients were non-Hispanic Whites and more than 90% were male in all consumption categories. The no-alcohol group was older than the high-risk alcohol group: 64 years vs 59.9 years ($P < .0001$). Compared with the high-risk alcohol group, the no-alcohol group had a significantly greater proportion of comorbid diabetes (62.3% vs 42.5%), hypertension (77.9% vs 69.1%), or cardiovascular disease (40.2% vs 25.9%, $P < .0001$ for all comparisons).

In a significant study observation, fewer than 5% of patients with high-risk use received behavioral or pharmacologic therapy and of those who did, most were referred for or received treatment at or near the time of cirrhosis diagnosis. "This highlights a major gap in linking patients with high-risk alcohol use to appropriate behavioral or pharmacologic therapy in a timely manner and may reflect missed opportunities to prevent further alcohol-related morbidity and mortality," Dr. Wong and colleagues wrote.

They called for studies of novel interventions for timely assessment of alcohol use with linkage to addiction services. They also cited the need to understand the interaction between levels of alcohol use and underlying MASLD.

This study received no specific funding. Dr. Wong reported funding through his institution from Gilead Sciences, Exact Sciences, and Thera Technologies. ■

Recent consensus in defining metabolic dysfunction-associated steatotic liver disease (MASLD) has raised awareness for the combined impact of cardiometabolic risk factors and alcohol consumption on liver disease progression. This study by Wong et al. highlights the undeniable influence of high-risk alcohol use on the development of advanced liver disease.


Dr. Wu

In a national cohort of over 1 million US veterans with steatotic liver disease (SLD), patients with high-risk alcohol use based on AUDIT-C assessment exhibited > 43% greater risk of cirrhosis compared to those with no alcohol use. The relationship between alcohol and liver severity in SLD was observed even after excluding patients meeting classification for predominant alcohol-associated liver disease. While increased alcohol use was associated with increased incidence of cirrhosis, decreased alcohol use led to a notable 39% reduction in cirrhosis risk over time.

Reducing alcohol consumption remains best practice guidelines for mitigating risk of progression in steatotic liver disease. However, results of this study emphasize the critical need for early identification and treatment of high-risk alcohol use in all patients with SLD. While universal recommendations for alcohol abstinence provides pragmatic implementation, there is a significant need to better understand the interaction of specific metabolic risk factors and patterns of alcohol use across the spectrum of MetALD to guide personalized recommendations for patient education and management.

Further research using prospective clinical trial design is needed to evaluate the interplay of alcohol consumption and metabolic risk factors across variable age, sex, genetics, and environmental exposures that are increasingly being recognized as vital drivers of health and disease.

Tiffany Wu, MD, MS, is a fellow in Transplant Hepatology at Mayo Clinic in Rochester, Minnesota. She has no conflicts.

AGA Defines Diagnostic, Treatment Approach to Cannabinoid Hyperemesis Syndrome

BY WILL PASS

FROM GASTROENTEROLOGY

A new American Gastroenterological Association (AGA) clinical practice update shines a light on cannabinoid hyperemesis syndrome (CHS).

CHS, which is triggered by chronic cannabis usage and manifests with GI and autonomic symptoms, is on the rise in the United States, yet underdiagnosis remains a challenge and clinical data are scarce, reported lead update panelist Alberto Rubio Tapia, MD, of Cleveland Clinic, Cleveland, Ohio, and colleagues.

"Although cannabis use has been reported for many decades, some of its unique adverse effects of nausea, vomiting, and abdominal pain, termed CHS, were noted relatively recently," the panelists wrote in *Gastroenterology* (2024 Mar 5. doi: 10.1053/j.gastro.2024.01.040). "The objective of this article was to help practitioners define the appropriate approach to the diagnosis and management of CHS."

According to the update, the typical CHS patient is male with a years-long history of daily or near-daily cannabis use. Paradoxically, while cannabis use drives this condition, some patients with CHS report that cannabis use relieves their symptoms.

The update describes CHS as a subtype of cyclical vomiting syndrome (CVS), and offers diagnostic criteria for CHS, reproduced below verbatim:

- **Clinical features:** stereotypical episodic vomiting resembling CVS in terms of onset, with frequency 3 or more times annually;
- **Cannabis use patterns:** duration of cannabis use more than 1 year before symptom onset; frequency more than 4 times per week, on average;
- **Cannabis cessation:** resolution of symptoms after a period of abstinence from cannabis use for at least 6 months, or at least equal to the total duration of 3 typical vomiting cycles in that patient.


Dr. Rubio Tapia

As CHS is a subtype of CVS, the update also provides an outline and management guide for this broader condition, which is characterized by four phases: inter-episodic, prodromal, emetic, and recovery.

During the inter-episodic phase, patients will have minimal or no symptoms, although almost one third will describe dyspepsia or nausea. Prophylactic medications in this period include tricyclics, mitochondrial supplements like CoQ10 and vitamin B12, NK1 antagonists, and anticonvulsants.

The prodromal phase is characterized by abdominal pain and nausea with a duration of 30-90 minutes. During this time patients may have autonomic symptoms like sweating and feeling hot or cold. Psychological symptoms may include feelings of panic and being "out of control." Abortive medications are appropriate during this period, according to the update, like triptans and antiemetics.

Next comes the emetic phase, in which patients exhibit "relentless vomiting," retching, abdominal pain, neurological symptoms and extreme thirst. Because an empty stomach may provide relief, inducing emesis may be considered, along with rest in a quiet dark room and supportive care.

Finally, the vomiting subsides during the recovery phase, when it is possible to restart oral intake and resume normal activities.

While this framework may be useful when managing patients with CHS, intervention should be centered around cannabis cessation, according to the update.

"For long-term management, counseling to achieve marijuana cessation and tricyclic antidepressants, such as amitriptyline, are the mainstay of therapy," Dr. Rubio Tapia and colleagues wrote.

Advising patients to stop cannabis "cold turkey" is not recommended, they added, as this may bring on withdrawal symptoms, and it tends to be ineffective in this population, which has a high recidivism rate.

"Co-management with a psychologist or psychiatrist may be helpful for patients who have a lack of response to standard therapies or extensive psychiatric comorbidity," the panelists wrote. "Anxiety and depression are very common associated conditions."

Dr. Rubio Tapia and colleagues concluded with a call for more research.

"Further understanding of CHS pathophysiology and evidence-based therapies are urgently needed," they wrote.

This update was commissioned and approved by the AGA. The update panelists disclosed relationships with Evoke Pharma, RedHill Biopharma, Takeda, and others. ■

AGA Update Describes High-Quality Upper Endoscopy

BY WILL PASS

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

American Gastroenterological Association (AGA) has published a clinical practice update detailing best practices for performing a high-quality upper endoscopy exam.

The update, authored by Satish Nagula, MD, of Icahn School of Medicine at Mount Sinai, New York, NY, and colleagues, includes nine pieces of best practice advice that address procedure optimization, evaluation of suspected premalignancy, and postprocedure follow-up evaluation.


Dr. Nagula

"Defining what constitutes a high-quality esophagogastroduodenoscopy (EGD) poses somewhat of a challenge because the spectrum of indications and the breadth of benign and (pre)malignant disease pathology in the upper GI tract is very broad," the update panelists wrote in *Clinical Gastroenterology and Hepatology* (2024 Feb 21. doi: 10.1016/j.cgh.2023.10.034). "Standardizing the measures defining a high-quality upper endoscopic examination is one of the first steps for assessing quality."

Preprocedure Recommendations

Dr. Nagula and colleagues first emphasized that EGD should be performed for an appropriate indication, citing a recent meta-analysis (Gastroenterology. 2022 Apr. doi: 10.1053/j.gastro.2021.12.270) that found 21.7% of upper endoscopy procedures were performed for an inappropriate indication. Of note, diagnostic yields were 42% higher in procedures performed for an appropriate indication.

After ensuring an appropriate indication, the update also encourages clinicians to inform patients of the various benefits, risks, and alternatives of the procedure prior to providing consent.

Intraprocedure Recommendations

During the procedure, endoscopists should take several steps to ensure optimal visualization of tissues, according to the update.

First, a high-definition (HD) white-light endoscopy system should be employed.

"Although HD imaging is a standard feature of newer-generation endoscopes, legacy standard-definition scopes remain in use," Dr. Nagula and colleagues noted. "Moreover, to provide true HD image resolution, each component of the system (eg, the endoscope video chip, the processor, the monitor, and transmission cables) must be HD compatible."

This HD-compatible system should be coupled with image-enhancing technology to further improve lesion detection. In Barrett's esophagus, the panelists noted, image enhancement can improve lesion detection as much as 20%.

They predicted that AI-assisted software may boost detection rates even higher: "Computer-aided detection and computer-aided diagnosis systems for upper endoscopy are still in the early phases of development but do show similar promise for improving the detection and

Continued on page 18

Dupilumab for Eosinophilic Esophagitis: How Is it Improving Treatment?

BY MARILYNN LARKIN

The US Food and Drug Administration approvals of dupilumab (Dupixent, Regeneron/Sanofi) in 2022 for adults and children with eosinophilic esophagitis (EoE) affirmed the safety and efficacy of the drug, which is the first product indicated specifically for treatment of this disease.

The expanded approval for its use in kids aged 1 year and older, which occurred in late January, implies that clinicians can prescribe it for just about any patient with the immune disorder.

But is dupilumab right for everyone?

What the Trials Said

Dupilumab, given by injection, is a recombinant human immunoglobulin-G4 monoclonal antibody that inhibits interleukin 4 (IL-4) and IL-13 signaling.

The first approval for EoE, on May 22, 2022, for adults and children aged 12 years and older weighing at least 40 kg, was based on data from 321 participants in the first two parts of a three-part phase 3 trial involving patients with EoE despite 8 weeks of high-dose proton pump inhibitor (PPI) therapy and with substantial symptom burden.

At 24 weeks, histologic remission occurred in 60% of patients in Part A of the trial and 59% in Part B who received a weekly 300-mg dose of dupilumab compared with 5% and 6% taking placebo. Additionally, Part A and B participants taking the drug weekly experienced a 69% and 64% reduction in disease symptoms, respectively, vs 32% and 41% for placebo. The drug also outperformed placebo in reducing patients' esophageal eosinophilic counts and abnormal endoscopic findings.

Dr. Katz

The second approval, on January 25, 2024, for children aged 1 year and older weighing at least 15 kg, was based on data from a two-part, placebo-controlled trial involving 102 children, ages 1-11 years, with EoE. The study involved a 16-week treatment period and a 36-week extended period during which eligible children from the dupilumab group continued to receive their weight-based dose level and those who were on placebo switched to active treatment. The trial showed that a greater proportion of children taking the drug achieved histological remission.

Temper Expectations

Dupilumab is a "major advance for EoE that has to find its place but should be looked at with optimism and what I call tempered expectations," Philip Katz, MD, AGAF, professor of medicine in the gastroenterology division at Weill Cornell Medicine, New York City, said in an interview. "I've been using it since *The New England Journal of Medicine* paper was published about a year and a half ago (2022 Dec. doi: 10.1056/NEJMoa2205982), and as a slow adopter, I like it."

Dr. Katz and his colleagues have been prescribing dupilumab mainly for patients who haven't responded to other medications, mainly PPIs and steroids.

"We start people on it without stopping anything else," Dr. Katz said. "Then, as symptoms evolve and people have a positive response, we stop the other medications. For example, in one patient who did very well on the drug, we stopped his steroids and now, we're weaning him off his PPI. It's a process. This is not a disease where you can rush people."

The tempered approach is in part because of payer issues, he noted.

"It's very difficult to get it reimbursed in the US if you haven't tried something else first," Dr. Katz said. "And because it's still relatively new in this field, standard treatment is still used frequently."

Although Dr. Katz has had "incredible success" with dupilumab so far, "nothing should be considered a miracle drug," he said. "A couple of people have had injection reactions, and one person couldn't tolerate the drug. So, while it seems to have an excellent response rate, it's not 100%. Like any new drug, it will have to find its true success rate."

Taking a Step-Up Approach

Like Dr. Katz, Evan Dellon, MD, MPH, AGAF, director of the Center for Esophageal Diseases and Swallowing at the University of North Carolina at Chapel Hill, North Carolina, is enthusiastic about dupilumab.

"It's a boon to the field, and now, some real-world data are coming out and looking very much like the clinical trial data, which are reassuring," said Dr. Dellon, a coauthor of the NEJM paper.

It's been a "game changer," particularly for people who weren't doing well with their current treatments, he said. "In my practice, I've been seeing a lowish response rate for PPIs, and about 30%-40% not responding to topical steroids, since we don't have a standard formulation for that. The diet elimination therapy is effective if people can do it well and adhere to it. But there's a group of people who don't respond, and probably, a larger group who can't really do that treatment long term. So, the drug has been fantastic for those patients."

Although the drug is approved for patients aged 1 year and older with no caveats, "it's not the right medicine for every patient," he said. "Patients in the clinical trials had EoE for 5 years, many of them were treatment refractory, and just under half had dilations and strictures," he said. "They represent a certain group of patients."

Dr. Dellon is taking a "step-up approach" to EoE treatment, first trying the standard interventions — PPIs, steroids, and an elimination diet — that many patients respond to.

Continued on following page

Continued from page 11

characterization of upper GI tract neoplasia."

Beyond selection of best available technologies, the update encourages more fundamental strategies to improve visualization, including mucosal cleansing and insufflation, with sufficient time spent inspecting the foregut mucosa via anterograde and retroflexed views.

Where appropriate, standardized biopsy protocols should be followed to evaluate and manage foregut conditions.

Postprocedure Recommendations

After the procedure, endoscopists should offer patients management recommendations based on the endoscopic findings and, if necessary, notify them that more recommendations may be forthcoming based on histopathology results, according to the update.

Similarly, endoscopists should follow established surveillance intervals for future procedures, with modifications made as needed, based on histopathology findings.

Document, Document, Document

Throughout the update, Dr. Nagula and colleagues repeatedly emphasize the importance of documentation, from preprocedural discussions with patients through planned surveillance schedules.

However, the recommendations are clear about "weighing the practical implications" of "onerous" documentation, particularly photodocumentation requirements. For instance, the authors note that "there are some scenarios in which more rigorous photodocumentation standards during upper endoscopy should be considered, such as patients with risk factors for neoplasia," but at the very least "photodocumentation of any suspicious abnormalities, ideally with annotations, is strongly advised."

Moving Toward Quality Standardization for Upper Endoscopy

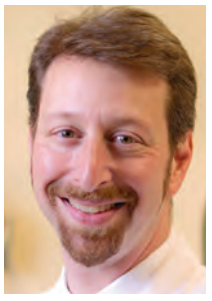
"These best practice advice statements are intended to improve measurable clinical, patient-reported, and economic healthcare outcomes and are not meant to put an additional burden on endoscopists," the panelists wrote. "Ideally, future research will set threshold indicators of adherence to these best practices that optimally are associated with these aforementioned objective outcomes."

This update was commissioned and approved by AGA. The update panelists disclosed relationships with Covidien LP, Fujifilm USA, Mahana Therapeutics, and others. ■

Continued from previous page

For new patients who choose medication therapy, he prescribes PPIs and then topical steroids and then steps up to dupilumab for patients who aren't responding or who have a strong preference for starting the drug early.

In addition to EoE, the drug is approved for certain patients with atopic dermatitis, asthma, and chronic rhinosinusitis with nasal polyposis. As such, Dr. Dellon said that he will try dupilumab early on in patients with multiple atopic conditions, such as asthma, eczema, or nasal disease.



Dr. Dellon

"Even if their EoE is not that severe, those patients can still benefit from a more streamlined systemic therapy," he said.

Questions Still Remain

Both Dr. Katz and Dr. Dellon pointed to dupilumab's cost and the related challenge of convincing insurance companies to cover the drug as major challenges to more widespread use. The lack of long-term data also poses a challenge.

Side effects, which often stand in the way of the use of a new drug, are not an issue, for the most part, at least in the short term, according to Dr. Dellon. The most common side effects are discomfort, redness at the injection site, and pain related to the injection.

"Keeping the medication out of the refrigerator to bring it up to room temperature can help, as can doing the injection in the lower abdomen," he said. "Otherwise, it's well tolerated, with no side effects that are unique to EoE."

Data from the third part of the clinical trial, which followed patients from weeks 24-52 of treatment, indicated that improvements in histological, symptomatic, endoscopic, and molecular features of EoE among patients taking weekly dupilumab continued or improved.

In my practice, "my observations have been that people are maintaining their responses," said Dr. Dellon.

However, one critical question is whether the dose intensity or frequency can be decreased over time without reducing the response rate.

"Hopefully, we'll start getting data on that in the next year or two," Dr. Dellon said. "It's hard to do that yet because the drug has only been out for a year or year and a half, and people are just getting to that year of the initial dosing."

Another question is how to use the drug in people who are different from the clinical trial population, such as those who have been responding to other therapies but want to switch, and people who are newly diagnosed but who have severe disease. Can the drug be used earlier in these populations?

Dr. Dellon would like to see a study that utilizes the new EoE index of severity metric to focus specifically on dupilumab use in patients with severe disease.

Early findings from his recent real-world study of 46 patients with severe disease who would not have qualified for the clinical trials found histologic, endoscopic, and symptom improvement in 91% of patients with refractory and fibrostenotic EoE after 6 months of dupilumab treatment.

While women tend to be well represented in the clinical trial, the drug needs to be tested in a more diverse population, Dr. Dellon noted. Research is underway looking at dupilumab effectiveness in people with different race/ethnicities.

EoE is more common among White people but that may be the result of a "detection issue," he said. "When clinicians see a Black or Hispanic patient with dysphagia, for example, they may not be thinking of EoE. And there are also some data suggesting that EoE presents slightly differently in non-White populations, which again could decrease the suspicion for it. This is an area we need to learn more about."

An 'Exciting' Drug

"We've got an exciting drug that is going to help a lot of people with a complex disease," Dr. Katz said. "But we should not forget that there are other interventions that have been successful, and quite frankly, they don't need to be abandoned."

"Learn about the drug if you've never used it," he advised. "Read the studies so you understand who the patients were as a baseline for where you're going to use it. Be prepared to do the appropriate paperwork requirements to get approvals from insurers. And look for more literature because it's coming."

Dr. Katz is a consultant to Phathom Pharma, Sebela Pharma, Medpace (not active), and Medtronic.

Dr. Dellon received research funding from Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, and Shire/Takeda. He served as a consultant to Abbott, AbbVie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, Eli Lilly, EsoCap, Eupraxia, Dr. Falk Pharma, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morphic, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, and Upstream Bio. He also received educational grants from Allakos, Aqilion, Holoclara, and Invea. ■

NEWS FROM AGA

Introducing Your 2024 AGA Recognition Prize Recipients

We are proud to announce the 2024 recipients of our annual recognition prizes, given in honor of outstanding contributions and achievements in gastroenterology and hepatology.

Congratulations to Bishr Omary, MD, PhD, for receiving AGA's highest honor, the Julius Friedenwald Medal. Presented annually since 1941, this award recognizes a physician for lifelong contributions to the field of gastroenterology. 2024 recognition prize recipients:

- **Julius Friedenwald Medal:** Bishr Omary, MD, PhD
- **William Beaumont Prize:** Hashem B. El-Serag, MD, MPH
- **Distinguished Achievement Award in Basic Science:** Jerrold R. Turner, MD, PhD, AGAF
- **Distinguished Service Award in Diversity, Equity, and Inclusion:** Sophie Balzora, MD
- **Distinguished Clinician Award in Private Practice:** Scott Ketover, MD, AGAF, FASGE
- **Distinguished Clinician Award in Academic Practice:** Shiv Kumar Sarin, MD
- **Distinguished Educator Award:** David Katzka, MD, AGAF
- **Distinguished Mentor Award:** John Pandolfino, MD
- **Young Investigator Award in Clinical Science:** Mingyang Song, ScD
- **Young Investigator Award in Basic Science:** Kathryn Hamilton, PhD

AGA

Investing in the Future of GI

aga research foundation

Talented young investigators are walking away from gastroenterology and hepatology research frustrated by a lack of support. For the last decades, Congress has slashed research funding and even greater cuts are on the horizon. Investigators in the early stages of their careers are particularly hard hit. Without help from other funding sources, young investigators struggle to continue their research, build their research portfolio, and obtain federal funding.

Decades of research have revolutionized the care of many digestive disease patients. These patients, as well as everyone in the gastroenterology and hepatology fields — clinicians and researchers alike — have benefited from the discoveries of dedicated investigators, past and present.

Right now, creative young researchers are poised to make groundbreaking discoveries that will shape the future of gastroenterology and hepatology. Unfortunately, declining government funding for biomedical research puts this potential in jeopardy. We're at risk of losing an entire generation of researchers.

To fill this gap, the AGA Research Foundation invites you to support its mission by making a donation. Funds raised through the AGA Research Foundation will support the pipeline of new investigators' research careers, allowing them to make discoveries that could ultimately improve patient care and even cure diseases.

"I donated to the AGA Research Foundation to ensure the vitality of our specialty, and to fund the research of future generations of gastroenterologists. Funding from organizations like the AGA Research Foundation is crucial for young scientists and gastroenterologists to launch their careers," states Michael Camilleri, MD, AGAF, AGA Research Foundation Chair.

By joining others in supporting the AGA Research Foundation, you will ensure that young researchers have opportunities to continue their life-saving work. Learn more or make a contribution at www.foundation.gastro.org. ■

Check Out Our New Crohn's Disease Clinician Toolkit

Have you ever wished you could access all of our Crohn's disease resources in one place? We've compiled our Crohn's disease clinical guidance, continuing education resources, patient education, and FAQs into one convenient toolkit.

Toolkit includes clinical guidance on:

- Role of biomarkers for the management of Crohn's disease
- Medical management of moderate to severe luminal and perianal fistulizing Crohn's disease
- Diet and nutritional therapies in patients with IBD

Check it out at www.gastro.org/toolkit. ■

AI Poised to Alter Healthcare

Shark Tank *from page 1*

and assistant professor of medicine at Stanford (California) University.

Their marriage has brought a unique perspective, according to Dr. Elango. "There isn't a single day that goes by when she talks to me about the inefficiencies in healthcare, and then I say, 'this can be easily solved with a software solution,' " he said.

When they decided to try a startup, the two initiated conversations with healthcare providers to identify a key unmet need. "The common

Dr. Elango

Dr. Dhanasekaran

recurring theme was that medical billing was a problem, because of [insufficient] institutional knowledge, staff shortage, and inconsistencies with the payers," said Dr. Elango. During their presentation, the two noted that about 80% of claims include at least one coding error, and this leads to an estimated $125 billion in annual losses.

Generative AI presented a solution. "Automating the medical billing code [determination] from a clinical record became 10 times easier than what it was before. So I thought, I can build a product that actually brings in augmented analytics and generative AI and do something that is tremendously useful to physicians," he said.

The future goal is to make life easier for healthcare providers, according to Dr. Dhanasekaran. "As physicians, we went into medicine to talk with patients, but a lot of us are just typing away when patients are sitting in the room, because there are all of these requirements for documentation to get the billing so that we can get paid at the end of the day," she said.

Arithmedics aims to initially target small-group medical practices that are tech savvy. They will analyze a year's worth of claims for errors and resubmit claims for the past 3 months and split any additional revenue that ensues. They plan to expand to revenue cycle management companies and hospital systems. On the technology side, they will expand to data intelligence and integrate with electronic health records, and ultimately plan to charge 1%-2% of revenue.

The other Shark Tank finalists were:

- **Aspero Medical:** Balloon overtube that maximizes frictional properties to improve mucosal wall traction and anchoring consistency. (Voted 'fan favorite' by AGA Tech Summit attendees)
- **Aurora Medical Technologies:** Minimally invasive, guided, tissue-anchoring suturing system for complex endoscopic procedures.
- **Ergami Endoscopy:** Flexible overtube capable of automatic insertion and fixation in the colon, which could potentially eliminate sedation and prevent endoscopic injuries to the physician.
- **Lazurite:** Wireless surgical camera that eliminates the need for light or video cables, avoiding the associated fire, trip, and contamination hazards.

The judges were swayed by Arithmedics' practical solution to a widespread problem. "There is for sure a need in terms of inaccurate billing and billing codes that are wrong. There's lost revenue for physicians around that. So I think we were really focused from a judging standpoint on the fact that their solution was filling truly an unmet need," said judge Andrea Vossler, a managing director of Varia Ventures, which has partnered with AGA to launch and manage the GI Opportunity Fund, an AGA-member venture fund.

"We were really focused on how to assist physicians in terms of supporting their practices, and really changing what you're doing. I think AI has the ability to do that, so we liked that about the company," she added.

The company is an example of how AI is poised to alter healthcare, according to Ms. Vossler. "I think it's massive. I think we're at the very beginning of its impact on healthcare," she said.

Another judge had a similar view. "They won because there is a screaming need to fix billing. So, it's well known that lots of money is indeed lost in billing practices, which are stressful for office personnel and stressful for physicians. They can fulfill a long-standing need, and we thought that that was the success story," said Christopher Gostout, MD, emeritus professor of medicine at Mayo Clinic in Rochester, Minnesota.

Dr. Gostout offered advice for gastroenterologists and other physicians interested in starting tech companies. It's imperative to be a realist, he said. "Is there a real market for it, or [is it just] a niche market? Does your device have legs — can it expand and can evolve into other [spin-off] products? These are things you need to think about because one-offs or single-trick ponies are pretty hard to move along now," said Dr. Gostout.

He recommended that entrepreneurs apply for Small Business Innovation Research (SBIR) grants. "I think it's a great opportunity to bring in money and get the ball rolling."

Finally, he advised entrepreneurs to be thoughtful about their advisory groups. Founders may be tempted to find the highest profile names they can to give the business gravitas, but those big names may not have the best knowledge base to understand

'It's well known that lots of money is indeed lost in billing practices, which are stressful for office personnel and stressful for physicians. They can fulfill a long-standing need, and we thought that that was the success story.'

the problems that the technology is meant to address. "I've seen businesses fail because they went for marquee names that really were not helpful, and they didn't do their due diligence in seeking out really useful value. You don't need a lot of advisers, just a couple of really good ones," said Dr. Gostout.

The summit was sponsored by the AGA Center for GI Innovation and Technology.

Dr. Gostout has founded and advises AdaptivEndo and Lean Medical. He is a consultant to Boston Scientific. Dr. Dhanasekaran has no financial disclosures. Ms. Vossler is an employee of Varia Ventures, which is an investment partner to AGA. Dr. Elango is an employee of Arithmedics. ■

Member SPOTLIGHT

Diet and the Microbiome

Wellness *from page 1*

Q: Why did you choose GI?
Dr. Ketover: I was a medical student working on my pediatrics rotation at Children's Minnesota (Minneapolis Pediatrics Hospital). A 17-year-old young man who had Crohn's disease really turned this into my lifelong passion. The patient confided in me that when he was 11, he had an ileostomy. He wore an ileostomy bag for 6 years and kept it hidden from all his friends. He was petrified of their knowing. And he told me at the age of 17 that if he knew how hard it was going to be to keep that secret, he would've preferred to have died rather than have the ileostomy. That got me thinking a lot about Crohn's disease, and certainly how it affects patients. It became a very motivating thing for me to be involved in something that could potentially prevent this situation for others.

Today, we have much better treatment for Crohn's than we did 30 years ago. So that's all a good thing.


MNGI Digestive Health

Dr. Scott Ketover

Q: Wellness and therapeutic diets are a specific interest of yours. Can you talk about this?
Dr. Ketover: We talk about things like Cheetos, Twinkies — those are not real foods. I do direct patients to 'think' when they go to the grocery store. All the good stuff is in the perimeter of the store. When you walk down the aisles, it's all the processed food with added chemicals. It's hard to point at specific things though and say: this is bad for you, but we do know that we should eat real food as often as we can. And I think that will contribute to our knowledge and learning about the intestinal microbiome. Again, we're really at the beginning of our infancy of this, even though there's lots of probiotics and things out there that claim to make you healthier. We don't really know yet. And it's going to take more time.

Q: What role does diet play in improving the intestinal microbiome?
Dr. Ketover: When you look at people who are healthy and who have low incidence of chronic diseases or inflammatory conditions, obesity, cancer, we're starting to study their microbiome to see how it differs from people who have those illnesses and conditions and try to understand what the different constituents are of the microbiome. And then the big question is: Okay, so once we know that, how do we take 'the unhealthy microbiome' and change it to the 'healthy microbiome'?

The only method we currently have is fecal transplant for *Clostridioides difficile*. And that's just not a feasible way to change the

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microbiome for most people.

Some studies are going on with this. There's been laboratory studies done with lab animals that show that fecal transplant can reverse obesity.

Q: Describe your biggest practice-related challenge and what you are doing to address it.

Dr. Ketover: The biggest challenge these days for medical practices is the relationship with the payer world and prior authorization. Where we've seen the greatest impact of prior authorization, unfortunately, is in the Medicare Advantage programs. Payers receive money from the federal government on plans that they can better manage the patient on, rather than Medicare. That results in a tremendous amount of prior authorization.

I get particularly incensed when I see that a lot of payers are practicing medicine without a license and they're not relying on the professionals who are actually in the exam room with patients and doing the history and physical examination to determine what is an appropriate course of diagnosis or therapy for a patient.

It comes around every January. We have patients who are stable on meds, then their insurance gets renewed and the pharmacy formulary changes. Patients stable on various therapies are either kicked off them, or we have to go through the prior authorization process again for the same patient for the umpteenth time to keep them on a stable therapy.

How do I address that? It's in conversations with payers and policy makers. There's a lot going on in Washington, talking about prior authorization. I'm not sure that non-practitioners fully feel the pain that it delivers to patients.

Q: What teacher or mentor had the greatest impact on you?

Dr. Ketover: Phillip M. Kibort, MD, the pediatric physician I worked with as a medical student who really turned me on to GI medicine. We worked together on several patients and I was able to develop an appreciation for the breadth and depth of GI-related abnormalities and diseases and therapies. And I really got excited by the spectrum of opportunity that I would have as a physician to help treat patients with GI illness.

Q: What would you do differently if you had a chance?

Dr. Ketover: I'd travel more both for work and for pleasure. I really enjoy my relationships that I've created with lots of other gastroenterologists as well as non-physicians around policy issues. I'm involved in a couple of national organizations that talk to politicians on Capitol Hill and at state houses about patient advocacy. I would have done more of that earlier in my career if I could have.

Q: What do you like to do in your free time?

Dr. Ketover: I like to run, bike, walk. I like being outside as much as possible and enjoy being active. ■

LIGHTNING ROUND

Texting or talking?
Texting, very efficient

Favorite city in U.S. besides the one you live in?
Waikiki, Honolulu

Favorite breakfast?
Pancakes

Place you most want to travel to?
Australia and New Zealand

Favorite junk food?
Pretzels and ice cream

Favorite season?
Summer

How many cups of coffee do you drink per day?
2-3

If you weren't a gastroenterologist, what would you be?
Public policy writer

Who inspires you?
My wife

Best Halloween costume you ever wore?
Cowboy

Favorite type of music?
Classic rock

Favorite movie genre?
Science fiction, space exploration

Cat person or dog person?
Dog

Favorite sport?
Football — to watch

What song do you have to sing along with when you hear it?
Bohemian Rhapsody

Introvert or extrovert?
Introvert

Optimist or pessimist?
Optimist

GLP-1 RAs Linked With Reduced CRC Risk in Patients With T2D

BY CAROLYN CRIST

Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) are associated with a reduced risk for colorectal cancer (CRC) in patients with type 2 diabetes, with and without overweight or obesity, according to a new analysis.

In particular, GLP-1 RAs were associated with decreased risk compared with other antidiabetic treatments, including insulin, metformin, sodium-glucose cotransporter 2 (SGLT2) inhibitors, sulfonylureas, and thiazolidinediones.

More profound effects were seen in patients with overweight or obesity, "suggesting a potential protective effect against CRC partially mediated by weight loss and other mechanisms related to weight loss," Lindsey Wang, an undergraduate student at Case Western Reserve University, Cleveland, Ohio, and colleagues wrote in JAMA Oncology.

Diabetes, overweight, and obesity are known risk factors for CRC and make prognosis worse. Ms. Wang and colleagues hypothesized that GLP-1 RAs might reduce CRC risk compared with other antidiabetics, including metformin and insulin, which have also been shown to reduce CRC risk.

Using a national database of more than 101 million electronic health records, investigators conducted a population-based study of more than 1.2 million patients who had medical encounters for type 2 diabetes and were subsequently prescribed antidiabetic medications between 2005 and 2019. The patients had no prior antidiabetic medication use nor CRC diagnosis.

The researchers analyzed the effects of GLP-1 RAs on CRC incidence compared with the other prescribed antidiabetic drugs, matching for demographics, adverse socioeconomic determinants of health, preexisting medical conditions, family and personal history of cancers and colonic polyps, lifestyle factors, and procedures such as colonoscopy.

During a 15-year follow-up, GLP-1 RAs were associated with decreased risk for CRC compared with insulin (hazard ratio [HR], 0.56), metformin (HR, 0.75), SGLT2 inhibitors (HR, 0.77), sulfonylureas (HR, 0.82), and thiazolidinediones (HR, 0.82) in the overall study population. GLP-1 RAs also were associated with lower but not statistically significant risk than alpha-glucosidase inhibitors (HR, 0.59) and dipeptidyl-peptidase-4 (DPP-4) inhibitors (HR, 0.93).

In patients with overweight or obesity, GLP-1 RAs were associated with a lower risk for CRC than most of the other antidiabetics, including insulin (HR, 0.5), metformin (HR, 0.58), SGLT2 inhibitors (HR, 0.68), sulfonylureas (HR, 0.63), thiazolidinediones (HR, 0.73), and DPP-4 inhibitors (HR, 0.77).

Study limitations include potential unmeasured or uncontrolled confounders, self-selection, reverse causality, and other biases involved in observational studies.

Further research is warranted to investigate the effects in patients with prior antidiabetic treatments, underlying mechanisms, potential variation in effects among different GLP-1 RAs, and the potential of GLP-1 RAs to reduce the risks for other obesity-associated cancers, the researchers wrote.

The study was supported by the National Cancer Institute Case Comprehensive Cancer Center, American Cancer Society, Landon Foundation-American Association for Cancer Research, National Institutes of Health Director's New Innovator Award Program, National Institute on Aging, and National Institute on Alcohol Abuse and Alcoholism. Several authors reported grants from the National Institutes of Health during the conduct of the study. ■

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