

## UEG week and UEG journal: A strong scientific *liaison*

The United European Gastroenterology (UEG) Week has now become one of the critical meetings in the field of gastrointestinal (GI) and liver diseases globally. The first edition of UEG Week was held 30 years ago, in Athens. Since 1992, the interest towards UEG activities increased exponentially.<sup>1</sup> In fact, more than 13,000 people from 120 countries all over the world gathered in Barcelona for the UEG Week in 2019. In January 2020, SARS-CoV-2 epidemic changed the world,<sup>2</sup> and the whole program of UEG Week was offered remotely for two consecutive years. Notwithstanding the disruption caused by SARS-CoV-2, both virtual editions were successful with >11,000 online participants. A large number of abstracts were submitted to the UEG Week in 2020 (2788, with 1915 [69%] accepted) and 2021 (1966, with 1482 [74.2%] accepted). Of these abstract, 32 were subsequently accepted for publication as full papers in the UEG Journal,<sup>3</sup> which last impact factor has increased significantly to a new height of 6.866 (23/93 in the field of gastroenterology and hepatology).<sup>4</sup>

The 2022 edition of UEG Week is a milestone in the history of UEG. Firstly, we look forward to returning to face-to-face events. An impressive number of high-quality abstracts were submitted to this edition: 2701 (of which 1745 (75%) were accepted for a total of 245 oral presentation and 1500 poster presentation). Further, 54 video cases and 317 clinical cases were received and formally evaluated for presentation by the Scientific Committee. In agreement with the recent virtual editions, the high volume and high standard of submitted abstracts confirm that the UEG Week has now become the most important forum at which to present your best GI-related research, independent of its format. Secondly, that the return to Vienna coincides with the 30<sup>th</sup> edition of UEG week, a historic moment for our Society.

Awaiting the most cutting-edge research to be presented in Vienna, here we summarize the original articles presented at UEG Week in 2020/2021 and then published in the UEG Journal (Figure 1).

In a case-control study, Zaccari et al investigated risk factors for development of ampullary tumors.<sup>5</sup> Since the incidence of ampullary tumor is increasing, especially in younger adults, this study is particularly welcome. History of previous cholecystectomy (HR: 2.07) and chronic use of proton pump inhibitor (HR: 1.7) were independently associated with development of ampullary tumors. Interestingly,

cholecystectomy was associated with development of intestinal subtype, both adenomas and carcinomas, whereas proton pump inhibitors were associated with adenomas only. Aspirin was associated with a reduced risk. Whether aspirin may be useful in patients undergoing endoscopic resection for ampullary tumors, to prevent recurrence, should be investigated in prospective trials.

There is an ongoing debate on which could be the best surveillance strategy in patients with branch-duct intraductal papillary mucinous neoplasms (BD-IPMNs). A better risk stratification may improve patient's management and individualize surveillance. In a prospective, multicenter cohort including 832 patients under surveillance for BD-IPMNs, Overbeek et al<sup>6</sup> externally validated the Dutch-American Risk stratification tool (DART-1: <https://rtools.mayo.edu/DART/>), which was proposed to identify cysts at lower risk of developing worrisome features or high-risk stigmata. DART-1's discriminative ability (C-statistic 0.68) was similar to that in the development cohort (0.64–0.72), with moderate calibration. Thus, DART-1 may now be considered to identify patients with BD-IPMNs at lowest risk for developing worrisome features or high-risk stigmata with 3–5 years (i.e.: in whom reduce the intensity of surveillance).

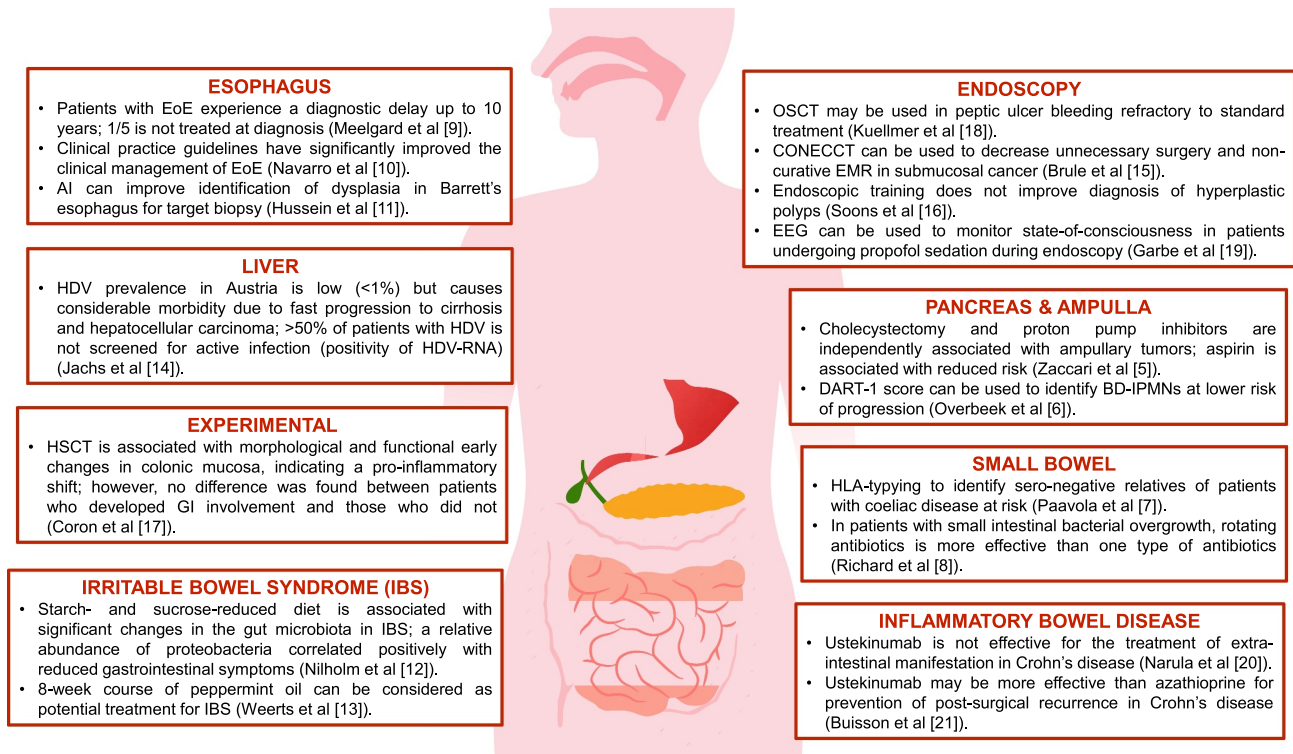
Counselling in relatives of patients with celiac disease may be challenging. In clinical practice, serological screening is widely used; yet, the need for, and the optimal timing of possible re-testing of seronegative “at-risk” individuals is unclear. To address this concern, Paavola and colleagues invited 599 screening-negative relatives of patients with coeliac disease to participate in a long-term follow-up study.<sup>7</sup> The overall incidence rate for later coeliac disease diagnosis or new seropositivity was 221/100,000 person-years; however, the incidence increased to 336/100,000 in patients with HLA at-risk. Therefore, HLA-typing seems a promising marker for identification of relatives who could benefit from re-testing.

Small intestinal bacterial overgrowth (SIBO) is a common issue in GI clinical practice, especially in female patients, and is associated with impaired quality of life and extensive use of healthcare resources. Treatment is based on oral antibiotics; however, which is the optimal treatment of SIBO is unknown. In a retrospective study including 223 patients with SIBO, Richard et al demonstrated that, compared to patients who were treated with one type of antibiotics, those receiving *rotating* antibiotics (azole and quinolone) were more

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**FIGURE 1** UEG Week and UEG Journal: a strong scientific liaison. Abbreviations: EoE: eosinophilic esophagitis; HDV: hepatitis D virus; HSCT: hematopoietic stem cell transplantation; OSCT: over-the-scope clip; EMR: endoscopic mucosal resection

likely to achieve clinical remission (70% vs. 51%, respectively). Notably, remission was associated with a significant improvement in both quality of life and bloating.<sup>8</sup> The first author of this paper, Nicolas Richard, will receive the best paper award of UEG Journal during the UEG week.

Eosinophilic esophagitis (EoE) is a chronic, local, progressive, immune-mediated disorder characterized by symptoms of esophageal dysfunction and eosinophil-predominant inflammation. In the past 20 years, both prevalence and incidence of EoE have increased sharply. EoE commonly affects young individuals, and—if not adequately treated—may be associated with dysphagia and development of fibrotic strictures. Yet, EoE goes often unrecognized and a diagnostic delay of years is not uncommon (up to 10 years in a study from Denmark<sup>9</sup>). Notably, the same study showed that approximately one-fifth patients were not treated at time of diagnosis.<sup>9</sup> A series of clinical practice guidelines were recently developed to improve the knowledge and management of EoE. In a cross-sectional analysis of the international EoE CONNECT registry of EoE, Navarro et al investigated whether the diagnostic process of EoE was effectively improved by release of such guidelines. Interestingly, they found that duration of diagnostic process, percentage of patients with strictures at diagnosis, and severity of disease as assessed by patient-reported Dysphagia Symptoms Score, were all significantly improved,<sup>10</sup> thus indicating that the European collaborative guidelines on EoE had a major positive impact on the management of these patients.

In patients with Barrett's esophagus, Seattle protocol biopsies (i.e. 4-quadrant biopsy specimens at intervals of every 1–2 cm

throughout the columnar-lined esophagus) are indicated to surveil for development of dysplasia. However, such protocol is labor intensive and the rate of dysplasia detection varies significantly. Hussein et al evaluated the use of convolutional neural networks (CNNs) to assist the endoscopists in identifying areas of dysplasia (i.e.: target biopsy).<sup>11</sup> Notably, the CNNs-guided approach allowed identification of areas for biopsy with excellent diagnostic accuracy (higher than six expert endoscopists). Pending further validation, these results support the application of artificial intelligence in daily life clinical practice.

Irritable bowel syndrome (IBS) is a chronic condition that affects millions of individuals worldwide. Signs and symptoms include cramping, abdominal pain, bloating, gas, and diarrhea or constipation, or both. IBS is not only associated with low quality of life and reduced work productivity, but also with significant use of health care resources. Therefore, there is an unmet need for trials investigating effective therapeutic approaches for patients with IBS. Starch- and sucrose-reduced diet (SSRD) is associated with improved symptoms in IBS. Interestingly, Nilholm et al showed that SSRD diet in IBS led to significant changes in the gut microbiota, thus suggesting that SSRD diet may be responsible for improved symptoms in these patients. More interestingly, a relative abundance of proteobacteria correlated positively with reduced GI symptoms.<sup>12</sup> As mentioned, increasing evidence indicates that diet significantly affects manifestation of IBS. In a multicenter, randomized controlled trials, Weerts et al assessed the cost effectiveness of peppermint oil to treat IBS.<sup>13</sup> She used data from a randomized clinical trial that demonstrated that 8-week

treatment with peppermint oil was associated with a (slight) improvement in quality of life, and abdominal pain. An economic evaluation showed that peppermint oil is a cost-effective treatment in patients with IBS.

We are now entering a new era for the treatment of hepatitis D virus (HDV) infection. Therefore, data on epidemiology and clinical impact of HDV in real-world clinical practice are particularly welcome. A multicenter study, mapped the current epidemiology of HDV in Austria.<sup>14</sup> They found a relatively low prevalence of HDV (<1% of patients with hepatitis B virus (HBV) chronic infection. However, most patients with HDV had active infection (i.e. positive HDV-RNA), which was associated with advanced liver disease, complications of clinically significant portal hypertension, and hepatocellular carcinoma in >50% of patients. Importantly, HDV-RNA was assessed in only 58% of anti-HDV positive patients. Interventions to improve screening for HDV active infection are urgently needed and will eventually help to stratify the priority for new drugs once available.

In large superficial colorectal lesions, optical diagnosis guides the modality for resection. The COlorectal NEoplasia Endoscopic Classification to Choose the Treatment (CONECCT) encompasses overt and covert signs of carcinoma, with the goal to identify adenomas with a high risk of superficial carcinoma (i.e.: lesions that have to be resected *en bloc* with free margins). In a prospective, multicenter study, Brule et al evaluated the diagnostic accuracy of CONECCCT classification for predicting submucosal invasion in colorectal lesions >20 mm. Accuracy of optical diagnosis before resection was compared with the final histological diagnosis. CONECCCT classification had sensitivity of 100%, specificity of 26.2%, positive predictive value of 11.6%, and negative predictive value of 100% for predicting submucosal adenocarcinoma. Therefore, the CONECCCT classification can be used to decrease unnecessary surgery and non-curative piecemeal endoscopic mucosal resection (EMR) in cases of submucosal cancer. The downside is the increased rates of not indicated endoscopic submucosal dissections for benign lesions.<sup>15</sup>

In 2016, the Workgroup Serrated Polyps and Polyposis (WASP) developed a classification system for endoscopic differentiation of adenomas, hyperplastic polyps and sessile serrated lesions. Soons et al evaluated: (1) whether a specific training endoscopists in applying WASP criteria on videos of polyps obtained with iScan could be associated with improved diagnosis; (2) if WASP criteria are still useful when polyps are pathologically revised according to the World Health Organization 2019 criteria. They found that: (1) training did not improve diagnosis; (2) after pathological revision of polyps according to 2019 criteria, diagnostic accuracy of all polyps significantly changes, thus suggesting that WASP 2016 classification may need revision.<sup>16</sup>

Allogenic hematopoietic stem cell transplantation (HSCT) may be a life-saving treatment.<sup>17</sup> However, post-transplant course is frequently characterized by development of graft-versus-host-disease (GVHD), which may be associated with significant morbidity and mortality. In patients with GVHD, the gastrointestinal tract may be involved in up to 60% of patients (i.e. acute digestive GVDH, aDGVHD). Pathophysiology of aDGVHD has not been thoroughly understood yet; however, intestinal mucosa has been

identified as a potential key player in the pathophysiology of GVHD initiation. Coron et al meticulously evaluated the changes in colonic mucosa in patients who underwent HSCT. Compared to controls, transplanted patients showed multiple morphological and functional changes of the colonic mucosa such as increased perimeter of colonic crypts and lower crypts sphericity, roundness, and mean vessel area. Interestingly, levels of interleukin-6, IL-33, and IL-15 in the supernatants of 24 h explant cultures of colonic biopsies were significantly increased in HSCT patients compared to controls, indicating a pro-inflammatory shift. Surprisingly enough, however, no difference was found between morphological parameters, intestinal permeability, and inflammatory cytokines between patients who actually developed aDGVHD and those who did not.

Over-the-scope clips (OSCT) can be used to treat peptic ulcer bleeding refractory to standard endoscopic treatment. By propensity matching, Kuellmer et al retrospectively compared safety and efficacy of OTSC ( $n = 66$  patients) versus transcatheter arterial embolization ( $n = 62$  patients) for the treatment of ulcer bleeding refractory to endoscopic hemostasis.<sup>18</sup> Notably, despite similar clinical characteristic, ulcers in the embolization group were larger, more often located in the duodenal bulb, and more frequently Forrest Ia, thus introducing a selection bias. Clinical success rate was comparable between the 2 groups, whereas duration of ICU admission and in-hospital mortality were both significantly lowered in patients who were treated by OSCT. In confirmed by randomized controlled studies, treatment with OSCT may become the first choice in ulcer bleeding refractory to standard therapy.

Objective methods to measure sedation depth in patients undergoing endoscopies are not yet available. In a proof-of-concept study, Garbe et al evaluated the potential use of EEG to monitor consciousness in patients receiving propofol for endoscopic procedures.<sup>19</sup> In agreement with previous data in patients undergoing general anesthesia, state-of-consciousness prediction with EEG parameters was feasible. Diagnostic accuracy was comparable between propofol sedation and general anesthesia. The area under the curve (AUC) ranged from 0.51 to 0.82 with complexity and optimized frequency domain parameters yielding the best results (AUC: 0.78–0.82). However, there was a considerable number of artefacts, which limits clinical application.

Ustekinumab (UST) may be effective for the treatment of extra-intestinal manifestations (EIM) in inflammatory bowel disease. Yet, studies are limited due to retrospective design, small sample size, and lack of control groups. In a post-hoc analysis of 3 clinical trials (NITI-1, UNITI-2, and IM-UNITI) investigating UST in patients with moderate to severe Crohn's disease (CD), Narula et al evaluated efficacy of UST for treatment of EIM.<sup>20</sup> Notably, the overall rate of EIM resolution was comparable between UST and placebo at week 6 (36.9% vs. 39.1%) and 52 (76.4% vs. 80%); in the sub-analysis evaluating the efficacy of UST according to the type of EIM, only erythema nodosum was significantly improved at week 52 of treatment. Awaiting confirmation by controlled studies using validated techniques with assessments performed by trained physicians, these data indicate that UST is not effective for the treatment of EIM in CD.

Buisson et al compared efficacy of UST versus azathioprine (AZA) in preventing post-surgical resection in patients with CD.<sup>21</sup> By propensity matching with inversed probability of treatment weighting, they compared 32 UST-treated patients versus 31 AZA-treated patients. The propensity score analysis was adjusted on the main risk factors such as smoking, fistulizing phenotype, prior bowel resection, resection length >30 cm and  $\geq 2$  biologics before surgery and AZA or UST exposure prior to surgery. Notably, the rate of endoscopic recurrence at 6 months after surgery was significantly lower in patients treated with UST versus AZA (28.0% vs. 54.5%); however, the rate of severe recurrence (Rutgeerts' index  $\geq i3$ ) was comparable between groups (16.9% vs. 27.9%). These results suggest that UST may be more effective than AZA in preventing post-operative recurrence; however, further confirmation by prospective randomized trials is needed.

In conclusion, a strong scientific *liaison* exists between the UEG community, especially the UEG week, and the UEG Journal. On the one hand, since its first edition in 1992, the UEG Week has now become the pivotal forum for presentation of GI-related research. On the other hand, the UEG Journal aims to high-quality, clinically relevant studies that will advance the knowledge and clinical management of patients with GI and liver disease.<sup>4</sup> Researchers in the field of gastroenterology and hepatology are therefore encouraged to continue submitting, presenting, and discussing their best research at the UEG Week.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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## DATA AVAILABILITY STATEMENT

Research data are not shared.

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