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December
2020

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President Message

Welcome to our December 2020 Newsletter!

Sad to say, 2020 is a tough year for a lot of people. Since the outbreak of COVID-19, we are forced to get used to new norms in daily life – wearing a face mask, social distancing, restriction on group gathering, everything online...to minimize close contacts between people. Many scientific meetings have also gone virtual then. For us, the Society organized online scientific meetings in June, September and October this year to continue to promote the advancement of gastroenterology. While we are still fighting the disease and facing lots of uncertainties in the coming months, we hope that everyone does his part, the months-long restrictions will come to an end and we will have our life back to normal.

On behalf of the Society, I would like to thank Professor Justin C.Y. Wu for organizing the 22nd Joint Annual Scientific Meeting, Professor Wai-Keung Leung for editing the two newsletters, Dr. Loey L.Y. Mak, Dr. Chun-Yu Say, Dr. Cyrus T.Y. Tse and Dr. Simon K.H. Wong for their scientific updates in this newsletter. Last but not least, all the sponsors who rendered support and contributions to the Society throughout the year.

The next newsletter will be published in June 2021.

Best wishes for a merry Christmas and a happy new year. Hope you are all healthy and safe.

Dr. Jodis T.W. Lam
President, The Hong Kong Society of Gastroenterology

Scientific Updates

Managing hepatitis B virus infection: New markers and treatments

Dr. Loey Lung-Yi Mak
Clinical Assistant Professor
Department of Medicine
The University of Hong Kong
Hong Kong

Commonly used biomarkers tend to underestimate disease activity

Chronic hepatitis B (CHB) infection is accompanied by the risk of progression to liver fibrosis, cirrhosis, hepatocellular carcinoma (HCC) or liver failure.[1] The natural course of chronic hepatitis B virus (HBV) infection follows a series of clinical phases, which include clinically important hepatitis B e antigen (HBeAg)-positive and HBeAg-negative serology phases.[1]

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ALT=alanine aminotransferase; TDF=tenofovir disoproxil fumarate.

References: 1. Vemlidy Hong Kong Prescribing Information (HK-FEB19-US-FEB19) **2.** Chan HLY, Lim YS, Seto WKW, et al. 3-year efficacy and safety of tenofovir alafenamide compared with tenofovir disoproxil fumarate in HBeAG-negative and –positive patients with chronic hepatitis B. The Annual Meeting of the American Association for the Sstudy of Liver Diseases (AASLD): The Liver Meeting®. San Francisco, California, USA. 9-13 November, 2018. Abstract 0381. **3.** Chan HLY, Marcellin P, Pan CQ, et al. No resistance to tenofovir alafenamide detected through 144 weeks of treatment in patients with chronic hepatitis B. The Annual Meeting of the American Association for the Study of Liver Diseases (AASLD): The Liver Meeting® 2018. San Francisco, November 9-13, 2018. Abstract 0386.

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Before prescribing, please consult full prescribing information which is available upon request.

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Apart from HBeAg positivity, HBV deoxyribonucleic acid (DNA) and serum alanine aminotransferase (ALT) levels are commonly used for disease monitoring because their fluctuations reflect hepatitis flares, followed by necroinflammation.[1] These markers are also used to assess antiviral treatment efficacy.[1] Since HBV cannot be completely eradicated due to the presence of covalently closed circular DNA (cccDNA) and integrated DNA in infected hepatocytes, treatment goals are to ensure a high degree of virologic suppression that could result in biochemical remission (ie, ALT normalization), improve hepatitis activity and reduce the risk of complications.[1-3]

However, existing markers cannot accurately predict clinical outcomes in patients treated with antiviral therapy.[4] Studies have revealed that a substantial proportion of patients with persistently normal ALT levels had significant fibrosis or inflammation on histology.[5] Also, viral transcriptional activities, seen as detectable serum HBsAg and intrahepatic HBV DNA, cccDNA and pregenomic ribonucleic acid (pgRNA), persist in patients with undetectable serum HBV DNA.[6] More accurate biomarkers are therefore needed for risk stratification.

Hepatitis B core-related antigen: A potential surrogate marker of cccDNA

As quantification of cccDNA requires a liver biopsy, non-invasive alternatives are being studied. Hepatitis B core-related antigen (HBcrAg) is a new serological marker that reflects intrahepatic transcriptional activity and is a surrogate marker for intrahepatic cccDNA, which is useful for monitoring and prognostication of CHB.[2,7]

HBcrAg consists of three related proteins, one of which is the hepatitis B core protein, i.e., a structural component of the viral capsid; the other 2 proteins are the HBeAg and the core-related protein (p22Cr).[2] It correlates well with intrahepatic HBV DNA, serum HBV DNA and HBsAg levels and may still be detectable when serum HBV DNA levels are undetectable or HBsAg seroclearance has been achieved.[2]

Studies have reported that HBcrAg is a strong predictor of HCC development.[8-10] A high HBcrAg level in nucleos(t)ide analog (NA) treatment-naive and treatment-experienced CHB patients was associated with an increased risk of HCC development.[9,10]

Moreover, HBcrAg also predicts the risk of HBV reactivation in patients receiving rituximab or allogeneic hematopoietic stem cell transplantation and the risk of HCC recurrence after curative treatment of HCC.[11,12]

Serum HBV RNA: A clinical marker for NA therapy monitoring

HBV RNA is only produced from cccDNA by transcription and is detectable in the serum as virions that contain primarily full-length pgRNA, encapsidated by core protein. It is correlated with serum HBV DNA and intrahepatic cccDNA in treatment-naive patients.[13]

Serum HBV RNA is present in all patients with CHB but at significantly lower levels than HBV DNA.[13,14] However, serum pgRNA levels are higher than HBV DNA levels in most patients receiving NA treatment because NAs block HBV replication by inhibiting the downstream reverse transcription but cannot directly inhibit the generation of HBV pgRNA virions.[15]

Serum HBV RNA levels may be correlated with the risk of HBV viral rebound after NA treatment cessation. It is therefore a potential predictive marker of safe discontinuation of NA therapy.[13,16]

Current first-line HBV treatment is not reaching long-term goals

Existing treatments are effective at serum HBV DNA suppression and ALT normalization but they are associated with a low HBsAg seroclearance rate and a relatively high rate of virologic relapse after discontinuation.[1,3] Antiviral treatments can reduce the risk of clinical morbidity and mortality, but the absolute number of HCC-related liver transplantations or deaths has been reduced only slightly. There is even a rising trend in the need for liver transplants in HCC patients.[17,18] Hence, new treatments are necessary to achieve the long-term treatment goals in CHB.

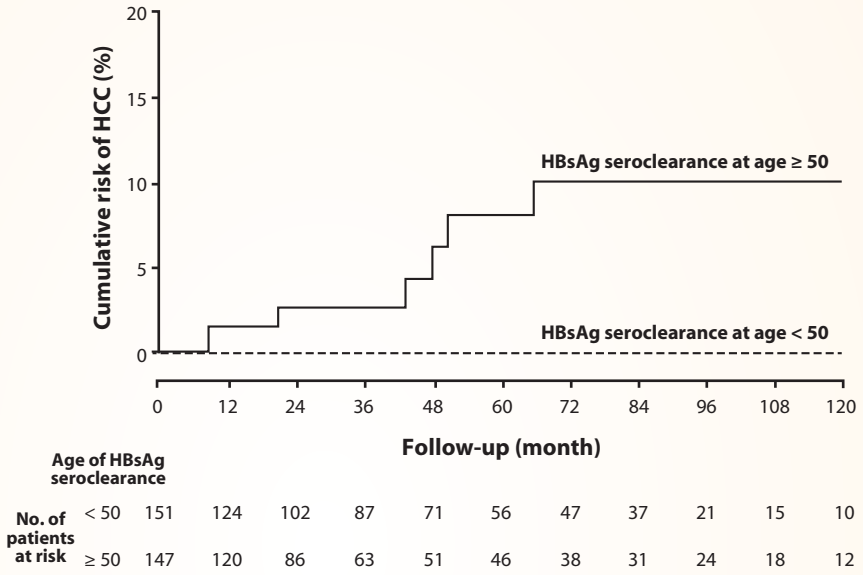
Novel drugs to enhance functional cure rates are in development

Although sterilizing cure (elimination of all viral particles including integrated DNA) or complete cure (elimination of cccDNA) cannot be achieved with current treatments, functional cure (HBsAg clearance with or without seroconversion) is of clinical importance and is a feasible treatment goal for CHB.[19]

Functional cure occurring at a young age (<50 years old) versus an older age is associated with a lower risk of future HCC development and complications (Figure).[20] It also leads to regression of fibrosis as well as reduction of clinical events, eg, liver decompensation, liver transplantation and/or death.[21] When functional cure is achieved, antiviral treatment, which should otherwise be continued long term, can be stopped.[20]

A number of new agents aiming to enhance functional cure rates are undergoing clinical assessment.

Figure. Cumulative risk for the development of HCC in patients achieving functional cure at <50 and ≥50 years of age[20]



Age of HBsAg seroclearance											
No. of patients at risk	< 50	151	124	102	87	71	56	47	37	21	15	10
	≥ 50	147	120	86	63	51	46	38	31	24	18	12

Functional cure is defined as HBsAg clearance with or without seroconversion.
HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma

Virus-directed agents may enhance functional cure rates

Gene silencers

Gene-silencing therapies that are based on RNA interference (RNAi) directly target HBV transcripts with high specificity, thereby reducing the production of viral proteins, which in turn ameliorates immune exhaustion and promotes host immune reconstitution.[22]

Core protein allosteric modulators

Core protein allosteric modulators (CpAM) block multiple steps in the HBV lifecycle to suppress HBV DNA, pgRNA and cccDNA. Combination treatment with a CpAM and NA may lead to deeper virologic suppression and has the potential to improve treatment of CHB.[23]

The effects of RNAi and CpAM therapies in CHB patients are summarized in the Table.

An ongoing trial of triple therapy combining an RNAi, CpAM and NA has shown promising results in terms of reductions in HBsAg and HBV DNA levels. The long-term results are pending.[24]

Table. Overview of virus-directed agents

	Evidence of target engagement			Ongoing effects after therapy cessation
	HBV RNA	HBsAg	HBcrAg	
RNAi	Yes	Yes	Yes	Yes (post-dosing ongoing HBsAg reduction and late HBsAg loss)
CpAM	Yes	No	No	No

CpAM, core protein allosteric modulator; HBcrAg, hepatitis B core-related antigen; HBsAg, hepatitis B surface antigen; HBV RNA, hepatitis B virus ribonucleic acid; RNAi, RNA interference

Conclusion

HBcrAg and HBV RNA are new markers that are useful for predicting clinical outcomes in CHB infection, such as HCC development or virologic relapse after cessation of antiviral treatment. The current first-line treatments for HBV infection provide effective virologic suppression but cannot entirely achieve the long-term goals of CHB management. Clinical trials of novel treatments are underway to identify agents that will enhance functional cure rates and reduce off-treatment disease progression.

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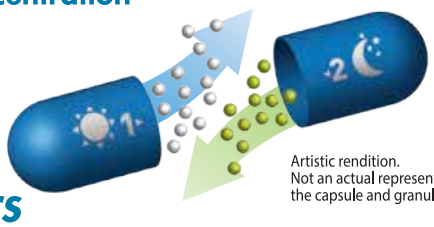

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Presentation & Packing: DR cap 30 mg 14's. 60 mg x 14's. **Contents:** Dexlansoprazole **Indications:** Healing & maintenance of all grades of erosive esophagitis. Treatment of heartburn associated w/ symptomatic non-erosive GERD. **Dosage:** Erosive esophagitis 60 mg once daily for 8 wk. **Maintenance:** 30 mg once daily. Symptomatic non-erosive GERD 30 mg once daily for 4 wk. **Administration:** Swallow whole. Alternatively, cap may be opened & entire contents sprinkled in a tbsp of applesauce. Swallow immediately w/o chewing. Cap may also be opened and granules can be administered w/ water in an oral syringe or via a nasogastric tube (≥16 French). **Contraindications:** Hypersensitivity & anaphylaxis. **Special Precautions:** Gastric malignancy, acute interstitial nephritis, B12 deficiency, hypomagnesemia, increased risk of GI infections & bone fractures. Concomitant use w/ methotrexate. Moderate & severe hepatic impairment. **Adverse Reactions:** Diarrhea, abdominal pain, nausea, upper resp tract infection, vomiting & flatulence. **Interactions:** Atazanavir, rilpivirine, digoxin, Fe salts, ketoconazole, warfarin, tacrolimus & rifampin.

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Clinical application of high-resolution manometry

Dr. Chun-Yu Say
Department of Medicine and Geriatrics
Caritas Medical Centre
Hong Kong

Diagnosis of esophageal motility disorders is often delayed or missed

Esophageal motility disorders (EMDs) are rare disorders of esophageal peristalsis and the lower esophageal sphincter (LES) characterized by symptoms of dysphagia, chest pain and regurgitation, although the symptoms are often poorly related to esophageal dysfunction.[1,2] Early diagnosis of EMD has major clinical significance because delayed diagnosis delays initiation of effective treatment leading to morbidity and impaired quality of life.[3]

The best-defined of the EMDs is achalasia, in which the LES fails to relax with swallowing and the esophageal body fails to undergo peristalsis.[1,2] Studies have revealed that there is a diagnostic delay for achalasia of 5 years on average.[3] Furthermore, 53% of patients with achalasia were prescribed proton pump inhibitors (PPIs) on the assumption that regurgitation and heartburn, which were reported in up to 68% of patients, were caused by gastroesophageal reflux disease (GERD).[3]

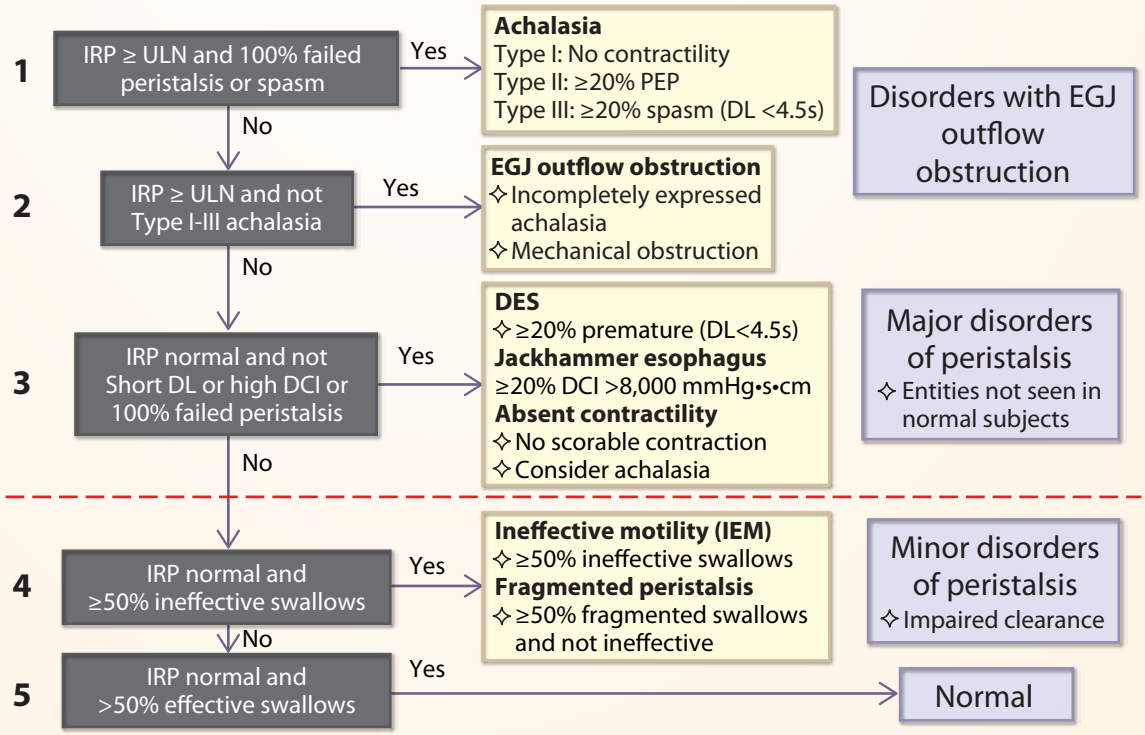
A barium contrast study was thought to be accurate in diagnosing achalasia, but an analysis (n=51) found that a correct diagnosis was missed in 42% of patients. Esophagogastroduodenoscopy has also been used to diagnose achalasia but lacks the sensitivity and specificity to achieve a definitive diagnosis.[4,5]

High-resolution manometry improves diagnosis and standardizes management of EMDs

Esophageal manometry is essential for assessing esophageal motor function in patients with EMDs. Emerging data suggest that high-resolution manometry (HRM) may have greater sensitivity for diagnosing achalasia than conventional manometry, and it has become the gold standard in evaluating EMD.[5]

The International HRM Working Group has developed an internationally recognized system – the Chicago Classification – to categorize EMD in patients with non-obstructive dysphagia and/or esophageal chest pain using standardized HRM metrics derived from pressure topography plots (Figure). The key metrics include the integrated relaxation pressure, distal contractile integral and distal latency.[6]

Figure. Hierarchical algorithm for the interpretation of HRM studies with Chicago Classification version 3.0[6]



DCI, distal contractile integral; DL, distal latency; DES, distal esophageal spasm; EGJ, esophagogastric junction; HRM, high-resolution manometry; IRP, integrated relaxation pressure; PEP, pan-esophageal pressurization; ULN, upper limit of normal

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2 Gross et al. Aliment Pharmacol Ther. 2006; 23(2): 303 – 12.

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The combination of HRM and the Chicago Classification prioritizes disorders of esophagogastric junction (EGJ) outflow (achalasia subtypes I–III and EGJ outflow obstruction [EGJOO]), other major disorders of peristalsis and minor disorders of peristalsis (Figure) so that treatment strategies can be optimized based on the phenotypes identified.[7]

Management of EMDs: Phenotype-directed treatment using HRM

Phenotyping EMDs has important management implications as each subtype has unique treatment considerations and a distinct optimal management strategy.

Achalasia

Achalasia, characterized by impaired LES relaxation and the absence of peristalsis, can occur as one of several disease phenotypes: type I or classic achalasia with low intraesophageal pressure; type II with pan-esophageal pressurization; and type III with high-amplitude spastic contractions. The best treatment response was uniformly seen in patients with type II achalasia (95%–96%) and the worst in type III achalasia (29%–70%).[8]

Common treatment options for most patients with achalasia include pneumatic dilation (PD), laparoscopic Heller myotomy (LHM) and peroral endoscopic myotomy (POEM). All these treatment modalities are efficacious for both type I and type II achalasia, but a low treatment success rate (40%) has been reported with PD in type III achalasia.[9] Although LHM and POEM are equally effective for patients with type III achalasia, POEM has emerged as the preferred treatment for this subtype.[9,10] Of note, a high rate of symptomatic GERD was observed after POEM (8.5%–47.5% of patients depending on measurement type), but most patients with post-POEM GERD respond to PPIs.[11]

EGJOO

EGJOO is diagnosed on HRM and defined as an incomplete LES relaxation with intact or weak peristalsis. Recent studies have found that many patients with EGJOO were minimally symptomatic or asymptomatic and up to 40% of cases resolved spontaneously. Botox injections are one of the first-line treatments, although the effect is usually short-lived.[8] A small minority of patients (~10%) may progress to achalasia, for which PD or POEM may be used.[12]

Spastic esophageal disorders

The Chicago Classification has grouped type III (spastic) achalasia, diffuse esophageal spasm (DES) and hypercontractile (jackhammer) esophagus together as spastic esophageal disorders (SEDs). Despite differences in pathophysiology, these disorders share many similarities in their clinical presentations, such as dysphagia, chest pain, regurgitation and/or heartburn. These disorders can be identified using HRM with esophageal pressure topography.[13]

The preferred treatment option for SEDs is POEM. In a retrospective study involving 73 patients who underwent POEM for SEDs, the clinical response rate was 93% during a mean follow-up of 234 days, and chest pain had significantly improved in 87% of patients after POEM.[13]

Minor disorders of peristalsis

Patients with normal and minor esophageal motor abnormalities report minimal symptoms and rarely progress over time. Minor motor disorders have an excellent prognosis and their clinical relevance is minimal.[14]

Role of HRM in GERD and hiatal hernia

HRM has a low predictive value for GERD and cannot be used as a diagnostic test. However, it is often used in the workup of patients with GERD symptoms that are unresponsive to symptomatic management and unexplained by endoscopy or barium studies. It is also used to exclude achalasia or a major motility disorder.[15]

Nevertheless, HRM is the most sensitive technique for detecting hiatal hernia because of its high sensitivity (92%) and specificity (95%), which exceed the sensitivity of endoscopy or barium studies alone (both 73%).[16]

Conclusion

HRM is considered the gold standard for diagnosing EMDs. Using HRM and the Chicago Classification together provides a standardized approach for analysis and categorization of abnormalities and allows optimization of EMD management.

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Current evidence in the management of rectal prolapse

Dr. Cyrus Tak-Yin Tse
Specialist in General Surgery
Private Practice
Hong Kong

Overview of rectal prolapse

Rectal prolapse is the protrusion of the rectal wall beyond the anus. Prolapse may be full thickness, partial thickness (mucosal) or internal prolapse (intussusception).[1] It is more common in women than in men, and risk factors for rectal prolapse include vaginal delivery, obesity, aging and constipation.[1]

Although not life threatening, rectal prolapse is a debilitating condition that has negative effects on quality of life (QoL). Depending on the severity of prolapse, symptoms include pain, bleeding, constipation, obstructed defaecation and faecal incontinence.[2]

Rectal prolapse is most commonly classified by the Oxford grading system after clinical or radiological assessment (Table).[2] The Cleveland Clinic Constipation Score (CCCS) and Faecal Incontinence Severity Index are other scoring systems often used for severity assessment.[2]

Clinical management of rectal prolapse

Most of the treatment options for rectal prolapse involve surgery, which can be performed through the anus (perineum) or the abdomen as either open or laparoscopic surgery.[3]

Table. Classification of rectal prolapse by the Oxford grading system

Oxford rectal prolapse grade		Characteristics of rectal prolapse
Internal rectal prolapse		
Rectal intussusception	Grade I	Descends no lower than the proximal limit of the rectocele
	Grade II	Descends into the level of the rectocele, but not to the anal canal
Rectoanal intussusception	Grade III	Descends to the top of the anal canal
	Grade IV	Descends into the anal canal
External rectal prolapse	Grade IV	Protrudes from the anus

Perineal approaches

Delorme mucosal sleeve resection

The Delorme procedure includes resection of the prolapsed mucosa and sutured plication of the bare muscle remnant, followed by mucosal reapproximation to seal the anastomosis.[4] It is usually reserved for old, frail patients with short, full-thickness prolapse because of a higher recurrence rate (10%–15%) versus abdominal procedures.[5,6] Some patients may have early complications, such as constipation, retention of urine, bleeding, etc, and the total complication rate is 4%–12%.[5,7]

Altemeier perineal rectosigmoidectomy

The Altemeier procedure involves a full-thickness resection of the rectum. It is a potential option for old and frail patients with comorbidities who are unsuitable for abdominal resection.[8] However, it is associated with a high recurrence rate (16%–30%) within 2 years and is no longer commonly performed.[9,10]

Stapled transanal rectal resection

In the stapled transanal rectal resection (STARR) procedure, staplers are used to perform a full-thickness rectal wall resection ultimately producing a circumferential transanal resection of the rectum.[11]

Stapled mucosectomy

Stapled mucosectomy involves transanal excision of internal mucosal prolapses using staplers.[12]

Abdominal approaches

Abdominal approaches can be open, robotic or laparoscopic. Currently, the majority of the procedures are performed laparoscopically.[13]

Rectopexy is a key component in the abdominal approach to rectal prolapse (level of evidence: I; grading of recommendation: A). A Cochrane systematic review recommended that the rectum be fixed rather than simply mobilized.[14]

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- A CONSISTENT AND FAVOURABLE SAFETY PROFILE[6,7]

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For further information, please consult full prescribing information.

Entyvio® (vedolizumab) 300 mg powder for concentrate for solution for infusion
Entyvio Abbreviated Prescribing Information:
Presentation & Packing: Powder for infusion (vial) 300mg x 1's. **Contents:** Vedolizumab I: treatment of adult patients with moderately to severely active Crohn's disease/Ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist. **Dosage:** For UC/CD: Entyvio 300mg IV infusion over 30 minutes at 0th, 2th week and 6th week then every 8 weeks thereafter. **Retreatment:** dosing at every 4 wk may be considered. **Contraindications:** Hypersensitivity. Active severe infections eg. TB, sepsis, cytomegalovirus, listeriosis & opportunistic infections eg. Progressive multifocal leukoencephalopathy. **Special Precautions:** Patients should be observed continuously during each infusion. Discontinue if a severe infusion-related reactions, anaphylactic reaction or other severe reaction occurs. Patients w/ controlled chronic severe infection or a history of recurring severe infections. Screen patients for TB before starting treatment. Increased risk of malignancy. Patients previously treated w/ natalizumab or rituximab. Concomitant w/ biologic immunosuppressants; live oral vaccines. May impair ability to drive or operate machinery. Women of childbearing potential should use adequate contraception. Pregnancy & lactation. **Adverse Reactions:** Nasopharynigitis, bronchitis, gastroenteritis, upper resp tract infection, influenza, sinusitis, pharynigitis, headache, paraesthesia, HTN, oropharyngeal pain, nasal congestion, cough, anal abscess & fissure, nausea, dyspepsia, constipation, abdominal distension, flatulence, haemorrhoids, rash, pruritus, eczema, erythema, night sweats, acne, arthralgia, muscle spasms, back pain, muscular weakness, fatigue, pyrexia. **Interactions:** Caution w/ concurrent use of live oral vaccines.

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Laparoscopic ventral mesh rectopexy
Laparoscopic ventral mesh rectopexy (LVMR) is the most commonly used technique and is considered the gold standard for managing rectal prolapse.[15]

During LVMR, part of the rectum down to the perineal body is mobilized and the rectum resuspended to the sacral promontory. A mesh, either synthetic or biological, is applied to the anterior wall to secure the position of the rectum.[15]

• *Functional outcomes of LVMR*
Functional outcomes in terms of faecal incontinence, obstructed defaecation and bladder and bowel dysfunction were evaluated in 58 female patients who underwent LVMR. After surgery, questionnaire scores for faecal incontinence (p=0.001), obstructed defaecation syndrome (p=0.001) and bowel and urinary symptoms (p=0.001) all improved significantly relative to baseline.[15]

A long-term outcome study (n=919) of LVMR, with a median postoperative follow-up of 33.9 months (range 0.4–143.6 months), showed a 10-year recurrence rate of 8.2%. Mesh-related complications were reported in 18 patients (4.6%), of which mesh erosion to the vagina occurred in seven patients (1.3%). Postoperative rates of faecal incontinence (11.1% vs 37.5%; p<0.0001) and obstructed defaecation (15.6% vs 54.0%; p<0.0001) improved significantly compared with preoperative incidence.[16]

• *LVMR for external versus internal prolapses*
Patients with external and internal prolapses showed similar results in terms of functional outcomes after LVMR, according to two systematic reviews. The weighted mean rates of improvement in faecal incontinence and constipation in patients with full-thickness rectal prolapse were 79.3% and 71%, respectively.[17] Similarly, the weighted mean rates of improvement in obstructed defaecation and faecal incontinence in patients with internal rectal prolapse were 73.9% and 60.2%, respectively.[18]

• *LVMR versus laparoscopic posterior sutured rectopexy*
LVMR demonstrated superior functional outcomes to laparoscopic posterior sutured rectopexy (LPSR) – a common abdominal procedure that does not use meshes. After a median follow-up of 6.1 years, patients who underwent LVMR (n=37) had significant improvements in constipation and QoL compared with those treated with LPSR. The QoL scores were 0.26 versus 0.93 (p=0.008) and total constipation symptom scores were 0.5 versus 1.0 (p=0.031), respectively. The obstructed defaecation score (p=0.011) and CCCS (p=0.017) also significantly favoured the LVMR group.[19]

• *Synthetic mesh versus biological mesh*
Meshes used in LVMR can be made from synthetic or biological materials. Synthetic meshes are more widely used than biological meshes during an LVMR because of their lower cost. Mesh erosion, a rare but serious complication, can occur through the rectum and the vagina, causing a long-lasting rectovaginal fistula or fulminant sepsis, noted Dr Tse.

Pooled data from prospective databases in five centres (n=2,203) and from eight studies (n=3,956) showed low incidence rates for mesh-related erosion after LVRM but the rates were slightly higher with synthetic versus biological meshes (2.4% vs 0.7% and 1.87% vs 0.22%, respectively). There is no strong consensus from surgeons on the optimal type of mesh to use.[20]

Conclusion
Rectal prolapse is a debilitating condition that adversely affects patient QoL. LVMR is an effective approach and the gold standard for the management of rectal prolapse. Perineal approaches are usually reserved for high-risk patients who are not suitable for abdominal surgeries. Regardless of the revision method selected, all patients should be counselled about risks for recurrence and complications before surgery is performed.

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* High quality of evidence: further research is very unlikely to change the confidence of the authors of the 2014 ACG monograph (Ford AC, et al. Am J Gastroenterol 2014) in the estimate of effect. Strong recommendation: recommendation that can apply to most patients in most circumstances and further evidence is unlikely to change the confidence of the authors of the 2014 ACG monograph (Ford AC, et al. Am J Gastroenterol 2014) in the estimate of treatment effect.

ACG = American College of Gastroenterology. CIC = chronic idiopathic constipation. GI = gastrointestinal. PEG = polyethylene glycol.

PRESENTATION AND FORM Powder for oral solution. Box of 10 or 20 sachets. **THERAPEUTIC INDICATION** FORLAX 10g is indicated in symptomatic treatment of constipation in adults and children aged 8 years and above. An organic disorder should have been ruled out before initiation of treatment. FORLAX® 10g should remain a temporary adjuvant treatment to appropriate lifestyle and dietary management of constipation, with a maximum 3-months treatment course in children. If symptoms persist despite associated dietary measures, an underlying cause should be suspected and treated. **DOSAGE AND ADMINISTRATION** The dosage is 1 to 2 sachets per day. The content of each sachet must be dissolved in a glass of water for oral consumption. The effect of FORLAX® becomes apparent within 24 to 48 hours after its administration. In children, treatment should not exceed 3 months. Treatment induced restoration of bowel movement will be maintained by lifestyle and dietary measures. In all cases, you must strictly comply with your doctor's prescription or your pharmacist's advice. **CONTRAINDICATIONS** Severe inflammatory bowel disease (ulcerative colitis, Crohn's disease), toxic mega colon, perforation or risk of perforation, ileus or suspicion of intestinal obstruction or symptomatic stenosis, painful abdominal syndromes of undetermined reason, and known hypersensitivity to FORLAX® or to one of the components. Due to the presence of sorbitol (traces), this medicine is contraindicated in persons who are intolerant to fructose. **DRUG INTERACTIONS AND OTHER INTERACTIONS FORLAX®** may interfere with the absorption of other drugs if administered simultaneously. Generally, it is better to take FORLAX® at least 2 hours apart from other products. **ADVERSE EFFECTS** Adverse Drug Reactions are listed under headings of frequency using the following categories: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); unknown (cannot be estimated from the available data). Adult population: The undesirable effects listed below have been reported during clinical trials (including 600 adult patients) and postmarketing use. Generally, adverse reactions have been minor and transitory and have mainly concerned the gastrointestinal system: **Adverse reactions: Gastrointestinal disorders (Common)** Abdominal pain and/ or distension, Diarrhoea, Nausea **(Uncommon)** Vomiting, Urgency to defecate, Fecal incontinence **Metabolism and Nutrition Disorders (Unknown)** Electrolytes disorders (Hyponatremia, Hypokalaemia) and or dehydration, especially in elderly patients **Immune system disorders (Very rare)** Hypersensitivity reactions (Pruritus, Rash, Face oedema, Quincke oedema, Urticaria, Anaphylactic shock) **Paediatric population**: The undesirable effects listed below have been reported during clinical trials including 147 children aged from 6 months to 15 years and post-marketing use. As in adult population, adverse reactions have generally been minor and transitory and have mainly concerned the gastrointestinal system: **Adverse reactions: Gastrointestinal disorders (Common)** Abdominal pain, Diarrhoea ***(Uncommon)** Vomiting, Bloating, Nausea Immune system disorders (Unknown) Hypersensitivity reactions **STORAGE CONDITIONS AND SHELF LIFE** To be stored below 25°C. Do not exceed the expiry date plainly indicated on the pack. Keep out of reach of children **Country of origin**: France

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Endoscopic sleeve gastroplasty – past and future

Dr. Simon Kin-Hung Wong
Consultant
Department of Surgery
Prince of Wales Hospital
The Chinese University of Hong Kong
Hong Kong

Weight loss intervention with endoscopic bariatric therapies

Bariatric surgery is an effective strategy for weight loss intervention. There is a consensus among physicians and surgeons in the Asia Pacific region that bariatric surgery should be considered for the treatment of obesity in Asian patients with a body mass index (BMI) ≥35 kg/m² with or without comorbidities; for patients with BMI ≥35 kg/m² with significant comorbidities; or patients with poorly controlled type 2 diabetes mellitus and a BMI ≥27.5 kg/m² despite lifestyle modifications and medical treatment.[1]

The most common bariatric surgery procedures are gastric bypass, sleeve gastrectomy, adjustable gastric band and biliopancreatic diversion with duodenal switch.[2] In recent years, endoscopic bariatric therapies have emerged as safer, less invasive alternatives for weight control compared with surgery. These endoscopic approaches can bridge the gap for patients who fail conservative or medical treatment and are reluctant or unsuitable to undergo surgery, noted Dr Wong.[3]

Endoscopic bariatric therapies attempt to mimic the mechanisms of conventional bariatric surgery, such as reducing effective gastric capacity (gastric restriction). This can be achieved by inserting space-occupying devices (intragastric balloon) or altering gastric anatomy using endoscopic suturing or plication devices (gastroplasty).[4]

In recent years, endoscopic treatment options have been evolving and various types of endoscopic gastroplasty have been developed. This article outlines the advantages and disadvantages of some of these procedures.

Endoscopic gastroplasty

Endoscopic stapling with transoral gastroplasty (TOGA)

TOGA is an incisionless, transoral restrictive bariatric procedure in which transoral endoscopically guided staplers are used to create a stapled restrictive pouch along the lesser curve of the stomach. The pouch is designed to invoke a sustained feeling of satiety after small meals.[5]

TOGA showed efficacy in terms of loss of excess BMI and body weight up to 1 year after the procedure in a single-arm trial,[5] but effectiveness was not consistently reported in randomized controlled trials. Moreover, because of its association with severe complications, such as perforations, this procedure has been abandoned by the developing company.

Endoscopic implant device with Transoral Endoscopic Restrictive Implant System (TERIS)

TERIS is a nonsurgical, endoscopic, gastric restriction procedure. With TERIS, a restrictive diaphragm is transorally implanted over the full-thickness transmural plication in the proximal portion of the stomach. The procedure is complex and associated with complications, such as pneumoperitoneum and perforation.[6] Dr Wong noted that, because of safety concerns, this technique is no longer performed.

Endoluminal vertical gastroplasty with endoscopic mucosal suturing system

Using the EndoCinch™ suturing system, the anterior and posterior faces of the gastric wall are sutured together to create an endoluminal vertical gastroplasty.[7] Two studies have shown notable weight loss with this procedure, but the plication and mucosal sutures were not durable.[8,9]

Primary obesity surgery endoluminal (POSE) procedure

In POSE, stomach tissue is plicated in various locations in the fundus and distal body using specialized suture anchors. The plicated areas mechanically restrict the volume of the stomach.[7] By reducing the gastric volume and delaying gastric emptying, this procedure aims to trigger earlier and prolonged satiety.[10]

In a study conducted in Spain, mean total weight loss was 16.6 kg and mean percentage loss of excess weight was 44.9% in 116 patients followed-up 12 months after POSE.[10] POSE demonstrated similar efficacy in a 12-month randomized controlled trial (n=44), with subjects who underwent POSE showing significant reductions in satiety parameters ($p<0.001$).[11]

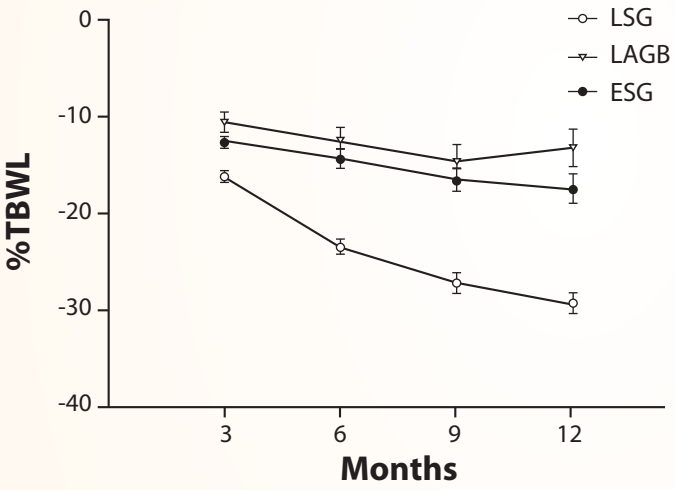
Endoscopic sleeve gastroplasty (ESG)

ESG is a transoral endoscopic gastric volume reduction procedure similar to sleeve gastrectomy. Using a flexible endoscopic suturing system (OverStitch™) that is mounted on a double-channel endoscope, a portion of the stomach is isolated by creating an uninterrupted series of full-thickness sutures along the length of the stomach approximating the anterior, greater curvature and posterior walls.[7]

In a case-matched study that compared ESG (n=105) and high-intensity diet and lifestyle therapy (HIDLT) alone (n=281), significantly more patients who underwent ESG had >20% total body weight loss (TBWL) than those with HIDLT at 12 months (55.8% vs 11.0%; $p<0.001$).[12] In addition, a multicentre study in moderately obese patients (n=248) also showed that ESG effectively induced weight loss, with a TBWL of 18.6% in 92 patients who were available for follow-up at 24 months.[13] More importantly, a meta-analysis of eight studies (n=1,772) found that weight loss after ESG was maintained at 12 months and 18–24 months with a TBWL of 16.5% and 17.2%, respectively.[14]

A single-centre, retrospective cohort study of obese patients (BMI >30 kg/m^2) compared the efficacy of ESG (n=91) with laparoscopic sleeve gastrectomy (LSG) (n=120) and laparoscopic adjustable gastric banding (LAGB) (n=67). Throughout the 12 months of follow-up, %TBWL was comparable in the ESG and LAGB groups (Figure), and there were no significant differences in %TBWL among the three different techniques for patients with BMI <40 kg/m^2.[15]

Figure. Percentage of total body weight loss during the 12-month follow-up period[15]



ESG, endoscopic sleeve gastroplasty; LAGB, laparoscopic adjustable gastric banding; LSG, laparoscopic sleeve gastrectomy; TBWL, total body weight loss

Conclusion

Despite the effectiveness of bariatric surgery, only a minority of morbidly obese patients are willing to undergo surgery. Bariatric endoscopy represents a less risky option that is more acceptable to patients. ESG is effective for weight loss and the results seem to be long lasting; however, more randomized controlled trials and further long-term outcome data are needed to confirm its efficacy and durability.

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Coming Soon

The Hong Kong Society of Gastroenterology
40th Annual General Meeting cum Scientific Meeting (Live Webinar)

Date: Tuesday, 9 March 2021, 8 pm

Organizing Chairperson: Dr. Wai-Fan Luk

Annual General Meeting

Presentation of Honorary Fellowship by President, Dr. Jodis T.W. Lam

Surveillance of gastric intestinal metaplasia finally coming of age

Professor Ernst J. Kuipers
Professor of Medicine
Department of Gastroenterology & Hepatology
Erasmus University Medical Centre
Rotterdam, The Netherlands

Case Presentation: Double-balloon enteroscopy assisted ERCP for patients with surgically altered anatomy

Dr. Ka-Shing Cheng
Associate Consultant
Department of Medicine
Tuen Mun Hospital
Hong Kong

(More information will be available soon from www.hksge.org)

Welcome! New Fellow & Member

Fellow

Dr. Ting-Ting CHAN
Department of Medicine & Therapeutics
Prince of Wales Hospital
Hong Kong

Member

Dr. Yu-Cheung CHENG
Departmenr of Medicine & Geriatrics
Princess Margaret Hospital
Hong Kong

22nd Joint Annual Scientific Meeting (Live Webinar)

Date: 6 September 2020

Organizing Chairperson: Professor Justin C.Y. Wu

Scientific Chairpersons: Professor Justin C.Y. Wu, Dr. Nelson N.S. Kung

Sponsored by: AbbVie, AstraZeneca, DCH Auriga, Ferring, Fresenius Kabi, Gilead, A.Menarini, Medtronic, Olympus, Otsuka, Pfizer Upjohn, Sandoz & Takeda

The 22nd Joint Annual Scientific Meeting (Live Webinar) was successfully held on 6 September 2020 and was attended by 183 healthcare professionals. The conference is an annual landmark scientific event jointly organized by six societies for gastrointestinal and hepatobiliary diseases in Hong Kong, namely The Hong Kong Society of Gastroenterology, Hong Kong Society of Digestive Endoscopy, Hong Kong Society for Coloproctology, The Hong Kong Association for the Study of Liver Diseases, The Hong Kong Society of Gastrointestinal Motility and Hong Kong IBD Society.

Due to the pandemic of COVID-19, the conference this year had gone virtual. Nevertheless, the program was stimulating and exciting as previous years. There were 6 lectures covered hot topics in gastroenterology, hepatology, endoscopy and surgery and were delivered by honorable local speakers included Dr. Simon K.H. Wong, Dr. Joyce W.Y. Mak, Dr. Michael K.S. Cheung, Dr. Chun-Yu Say, Dr. Loey L.Y. Mak and Dr. Cyrus T.Y. Tse.

Interactive panel discussions were held at the end of the each of the three symposia. Delegates participated actively throughout the discussions. This year's meeting continued to provide a valuable platform for local and overseas gastrointestinal professionals and experts to exchange knowledge and share experience in different perspectives of GI diseases. It was proven to be an enjoyable and rewarding event.

Major Meetings

3-5 December 2020
Gastro 2020 Prague
Organizers: World Gastroenterology Organisation,
The Czech Society of Gastroenterology
Location: Prague, Czech Republic
Website: www.gastro2020prague.org

16-18 December 2020
The 8th Annual Meeting of Asian Organization for Crohn's & Colitis (Hybrid)
Organizers: The Asian Organization for Crohn's & Colitis (AOCC) and Korean Association for the Study of Intestinal Diseases (KASID)
Location: Busan, Korea
Website: http://aocc2020.org/

18 December 2020
AASLD-CFHPC Digital Hepatology Connect
Organizers: The American Association for the Study of Liver Diseases (AASLD), The China Foundation for Hepatitis Prevention and Control (CFHP)
Website: https://achcc2020.sciconf.cn/cn/web/index/

4-6 February 2021
30th Annual Conference - Asian Pacific Association for the Study of the Liver (APASL 2021) – Hybrid Meeting
Organizer: The Asian Pacific Association for the Study of the Liver
Location: Bali, Indonesia
Website: http://apasl2021bangkok.org/

5-6 February 2021
Digital Liver Cancer Summit
Organizer: European Association for the Study of the Liver
Website: https://easl.eu/event/digital-liver-cancer-summit-2021/

3-5 Mach 2021
EURO EUS Congress 2021
Location: Santiago de Compostela, Spain
Website: www.euro-eus.org/

4-7 March 2021
Canadian Digestive Diseases Week (CDDW 2021) - Virtual
Host: Canadian Association of Gastroenterology
Location: Banff, Canada
Website: www.cag-acg.org/cddw

19-20 March 2021
The 29th Annual Meeting of the Korean College of Helicobacter and Upper Gastrointestinal Research & The 17th Korea-Japan Joint Symposium on Helicobacter Research (Hybrid)
Organizer: Korean College of Helicobacter and Upper Gastrointestinal Research, Japan Society for Helicobacter Research
Location: Seoul, Korea
Website: www.helicobacterkorea.org/

25-27 March 2021
ESGE Days 2021 (Virtual)
Organizer: European Society of Gastrointestinal Endoscopy
Website: www.esge.com/

31 March - 3 April 2021
14th International Gastric Cancer Congress (IGCC 2021)
Organizer: International Gastric Cancer Association
Location: Texas, USA
Website: www.igcc2021houston.com/

14-17 April 2021
FNM 2020 – 4th Meeting of the Federation of Neurogastroenterology and Motility and Postgraduate Course on Gastrointestinal Motility (Hybrid Conference)
Hosted by: Australian Neurogastroenterology & Motility Association, American Neurogastroenterology & Motility Society, Asian Neurogastroenterology & Motility Association and European Society of Neurogastroenterology & Motility
Location: Adelaide, Australia
Website: http://fnm2020.org.au/

24-28 April 2021
2021 American Society of Colon and Rectal Surgeons Annual Scientific Meeting (Hybrid Meeting)
Organizer: The American Society of Colon and Rectal Surgeons (ASCRS)
Location: California, USA
Website: https://fascrs.org

12-15 May 2021
The 2021 Biennial Conference of the International Society for Gastrointestinal Hereditary Tumours (InSiGHT)
Location: New Jersey, USA
Website: www.insight2021.org/

21-23 May 2021
Digestive Disease Week (DDW 2021) - Virtual
Sponsoring Societies: American Association for the Study of Liver Diseases (AASLD), American Gastroenterology, Association (AGA), American Society for Gastrointestinal Endoscopy (ASGE) and The Society for Surgery of the Alimentary Tract (SSAT)
Location: Washington D.C., USA
Website: www.ddw.org

12-13 June 2021
3rd World Congress of International Laparoscopic Liver Society (ILLS) 2021 – Virtual
Organizer: International Laparoscopic Liver Society
Website: https://ills2021.com/

17-20 June 2021
The 17th International Symposium on Viral Hepatitis and Liver Disease - Global Hepatitis Summit 2020/2021 (ISVHLD GHS 2020/2021)
Organizers: ISVHLD / GHS and the Taiwan Association for the Study of the Liver
Location: Taipei, Taiwan
Website: ghs2020taipei.com/

20-22 June 2021
The 38th Gastroenterology and Endotherapy European Workshop (GEEW)
Location: Brussels, Belgium
Website: www.live-endoscopy.com/

22-25 June 2021
EASL - The International Liver Congress 2021
Organizer: European Association for the Study of the Liver
Location: Amsterdam, The Netherlands
Website: easl.eu/event/the-international-liver-congress-2021-2/

30 June – 3 July 2021
2021 ESMO World Congress on Gastrointestinal Cancer
Organizer: European Society for Medical Oncology
Location: Barcelona, Spain
Website: www.worldgicancer.com/

7-10 July 2021
17th World Congress of Endoscopic Surgery & 29th International Congress of the European Association for Endoscopic Surgery
Hosted by: European Association for Endoscopic Surgery (EAES)
Location: Barcelona, Spain
Website: http://eaes.eu/wces2021/

7-10 July 2021
16th Congress of European Crohn's and Colitis Organization (ECCO) on Inflammatory Bowel Diseases
Organizer: European Crohn's and Colitis Organization
Location: Copenhagen, Denmark
Website: www.ecco-ibd.eu/ecco21.html

2-5 August 2021
Americas Hepato-Pancreato-Biliary Association 2021 Annual Meeting
Organizer: Americas Hepato-Pancreato-Biliary Association
Location: Florida, USA
Website: www.ahpba.org

19-21 August 2021
17th ISDE World Congress for Esophageal Diseases
Organized by: The International Society for Diseases of the Esophagus
Location: Toronto, Canada
Website: www.isde.net

19-22 August 2021
Asian Pacific Digestive Week (APDW 2021)
Organizer: Asian Pacific Digestive Week Federation (APDWF), Asia Pacific Association of Gastroenterology (APAGE), Asia Pacific Association for the Study of the Liver (APASL), Asian Pacific Society for Digestive Endoscopy (A-PSDE) and ISDS Asian Pacific
Location: Kuala Lumpur, Malaysia
Website: apdwkl2021.org

2-3 September 2021
APASL Single Topic Conference on Molecular & Cellular Biology
Organizer: Asian Pacific Association for the Study of the Liver
Location: Osaka, Japan
Website: www.apaslstc-osaka2021.org/

8-11 September 2021
The 8th Biennial Congress of The Asian-Pacific Hepato-Pancreato-Biliary Association
Hosted by: Indonesian Hepato-Pancreato-Biliary Association, Asian-Pacific Hepato-Pancreato-Biliary Association
Location: Bali, Indonesia
Website: https://aphpba2021.com/

2-6 October 2021
29th UEG Week
Organizer: United European Gastroenterology (UEG)
Location: Vienna, Austria
Website: www.ueg.eu

14-17 October 2021
19th International Celiac Disease Symposium (ICDS) 2021
Organizer: International Society for the Study of Celiac Disease
Location: Sorrento, Italy
Website: www.icds2021sorrento.com/

4-7 November 2021
Japan Digestive Disease Week (JDDW) 2021
Location: Kobe, Japan
Website: www.jddw.jp

25-28 November 2021
18th Congress of Asia Pacific Federation of Coloproctology (APFCP 2021)
Organizers: Asia Pacific Federation of Coloproctology, Society of Colon and Rectal Surgeons Taiwan, Asian Society of Stoma Rehabilitation
Location: Taipei, Taiwan
Website: www.apfcp2021.com/

12-15 December 2021
World Congress of Gastroenterology (WCOG) 2021
Organizer: The World Gastroenterology Organization
Location: Dubai, United Arab Emirates
Website: http://wcog2021.org/

(More information is available from www.hksge.org/events)

HKSGE Secretariat Suite 703, 7/F, Chinachem Johnston Plaza, 178-186 Johnston Road, Wanchai, Hong Kong
Tel: (852) 2869 5933 | Fax: (852) 2869 9533 | E-mail: gastro@hksge.org | Website: www.hksge.org

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EPCLUSA®
sofosbuvir/velpatasvir
400 mg/100 mg tablets

COVERAGE OF ALL GENOTYPES FOR CHC TREATMENT[1]

Just so
SIMPLE
12 WEEKS FOR ALL ELIGIBLE PATIENTS*†,[1]

Simple for You
- Up to 100% cure*,[1]
- Fixed Duration[1]
- PanPan (Pan-fibrotic, Pan-genotypic) single-tablet regimen‡,[1]

Simple for Them
- PI-free[1]
- No food restriction[1]
- One pill, once a day[1]

Proven in Real World
- Real-world experience with SOF-based regimens across the world[2-4,1]

* Achieving SVR12 is considered as cure by EASL. SVR12 is defined as undetectable HCV RNA at 12 weeks after cessation of treatment. Across the pivotal ASTRAL-1, -2 and -3 studies, cure rate of 95-100% were seen in HCV GT1-6 patients treated with 12-week EPCLUSA®. In ASTRAL-1, -2 and -3 studies, 1,035 patients with GT 1-6 HCV infection received 12 weeks of EPCLUSA® (SOF/velpatasvir 400 mg/100 mg). Patients (n=116) in the comparator arm of ASTRAL-1 received placebo, while 132 and 275 patients in the comparator arms of ASTRAL-2 and -3 respectively received SOF+RBV. Because of the low prevalence of HCV GT5 in the study regions, GT5 patients were assigned to the EPCLUSA® group in ASTRAL-1. Overall, 21% had compensated cirrhosis and 28% had failed prior treatments across three trials. Primary endpoint (SVR12 rates of 99%, 99% and 95% for ASTRAL-1, -2 and -3 respectively) were met by 98% of the patients.

† Unless otherwise clinically indicated, there is no need for baseline resistance or on-treatment monitoring of hematology and clinical chemistry in patients receiving EPCLUSA®. As a pangenotypic therapy, EPCLUSA® removes the need for genotypic testing prior to treatment. EPCLUSA®+RBV is recommended for the treatment of patients with decompensated cirrhosis, and may be considered for the treatment of HCV GT3 patients with compensated cirrhosis.

‡ Initial number of recruitment was 3,763 in HCV-TARGET[2] and TRIO network[3,4]. SVR12 rate was 96.1% (294/306) in overall treatments[2], and 91.5–98.1% (1398/1450 in total) across the genotypes 1–6[3,4]

CHC: Chronic hepatitis C; EASL: European Association for the Study of the Liver; GT: Genotype; HIV: Human immunodeficiency virus; HCV: Hepatitis C virus; PI: Protease inhibitor; RBV: Ribavirin; RNA: Ribonucleic acid; SOF: Sofosbuvir; SVR12: Sustained virologic response 12 weeks post-treatment.

References: 1. EPCLUSA® Hong Kong prescribing information (Version: HK-JUN17-EU-MAY17). 2. Land CS, et al. Safety and efficacy of velpatasvir and sofosbuvir-based regimens for the treatmemt of HCV genotype 1-6: Results of the HCV-TARGET Study. The 68th Annual Meeting of the American Association for the Study of Liver Diseases; The Liver Meeting® 2017, Washington, DC, October 20–24, 2017. 3. Curry M, et al. Sofosbuvir/velpatasvir compared to existing Standards of Care in GT2-6 HCV: Real-world experience from the TRID Network. The Annual Meeting of the European Association for the Study of the Liver: The International Liver Congress™ 2017, Amsterdam, the Netherlands, April 19-23, 2017. 4. Tsai N, et al. Utilization of DAA therapies (edipasvir/sofosbuvir and sofosbuvir/velpatasvir in patients with genotype 1 HCV: real-world experience from the TRIO Network, The Annual Meeting of the European Association for the Study of the Liver: The International Liver Congress™ 2017, Amsterdam, the Netherlands, April 19-23, 2017.

EPCLUSA® Abbreviated Prescribing Information (Version: HK-JUN17-EU-MAY17)
Presentation: Pink, diamond-shaped, film-coated tablet of dimensions 20 mm x 10 mm, debossed on one side with "GSI" and "7916" on the other side. **Indications:** Epclusa is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults. **Dosage:** Adults: one tablet, taken orally, once daily with or without food. Patients who have previously failed therapy with an NS5A-containing regimen: Epclusa with ribavirin for 24 weeks may be considered. Elderly: No dose adjustment is warranted for elderly patients. Renal impairment: No dose adjustment of Epclusa is required for patients with mild or moderate renal impairment. The safety and efficacy of Epclusa has not been assessed in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m2) or end stage renal disease (ESRD) requiring haemodialysis. Hepatic impairment: No dose adjustment of Epclusa is required for patients with mild, moderate, or severe hepatic impairment (CPT Class A, B, or C). Safety and efficacy of Epclusa have been assessed in patients with CPT Class B cirrhosis, but not in patients with CPT Class C cirrhosis. Paediatric population: The safety and efficacy of Epclusa in children and adolescents aged less than 18 years have not yet been established. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. Medicinal products that are potent P-glycoprotein (P-gp) or potent cytochrome P450 (CYP) inducers (rifampicin, rifabutin, St. John's wort [Hypericum perforatum], carbamazepine, phenobarbital and phenytoin). Co-administration will significantly decrease sofosbuvir or velpatasvir plasma concentrations and could result in loss of efficacy of Epclusa. **Warnings and Precautions:** Epclusa should not be administered concurrently with other medicinal products containing sofosbuvir. Severe bradycardia and heart block: Cases of severe bradycardia and heart block have been observed when sofosbuvir used in combination with another direct acting antiviral (DAA), is used with concomitant amiodarone with or without other medicinal products that lower heart rate. Amiodarone should only be used in patients on Epclusa when other alternative anti-arrhythmic treatments are not tolerated or are contraindicated. Patients who are identified as being at high risk of bradyarrhythmia should be continuously monitored for 48 hours in an appropriate clinical setting. Monitoring should also be carried out for patients who have discontinued amiodarone within the past few months and are to be initiated on Epclusa. All patients receiving Epclusa in combination with amiodarone with or without other medicinal products that lower heart rate should also be warned of the symptoms of bradycardia and heart block and should be advised to seek medical advice urgently should they experience them. Patients who have previously failed therapy with an NS5A-containing regimen: There are no clinical data to support the efficacy of sofosbuvir/velpatasvir for the treatment of patients who have failed treatment with a regimen containing another NS5A inhibitor. Treatment with Epclusa + RBV for 24 weeks can be considered for patients who have failed therapy on an NS5A-containing regimen and who are deemed at high risk for clinical disease progression and who do not have alternative treatment options. Renal impairment: No dose adjustment of Epclusa is required for patients with mild or moderate renal impairment. The safety of Epclusa has not been assessed in patients with severe renal impairment (eGFR < 30 mL/min/1.73 m2) or ESRD requiring haemodialysis. Use with moderate P-gp inducers or moderate CYP inducers: Co-administration of such medicinal products that are moderate P-gp or moderate CYP inducers (e.g. oxcarbazepine, modafinil or efavirenz) with Epclusa is not recommended. Use with certain HIV antiretroviral regimens: Patients receiving Epclusa concomitantly with elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate or with tenofovir disoproxil fumarate and a boosted HIV protease inhibitor should be monitored for tenofovir-associated adverse reactions. HCV/HBV (hepatitis B virus) co-infection: Cases of HBV reactivation, some of them fatal, have been reported during or after treatment with direct-acting antiviral agents. HBV screening should be performed in all patients before initiation of treatment. HBV/HCV co-infected patients are at risk of HBV reactivation, and should therefore be monitored and managed according to current clinical guidelines. CPT Class C cirrhosis: Safety and efficacy of Epclusa has not been assessed in patients with CPT Class C cirrhosis. Liver transplant patients: The safety and efficacy of Epclusa in the treatment of HCV infection in patients who are post-liver transplant have not been assessed. **Adverse reactions:** Headache, fatigue and nausea were the most common treatment emergent adverse events reported in patients treated with 12 weeks of Epclusa. Cases of severe bradycardia and heart block have been observed when sofosbuvir used in combination with another direct acting antiviral, is used with concomitant amiodarone and/or other medicinal products that lower heart rate. **Drug interactions:** Patients treated with vitamin K antagonists: As liver function may change during treatment with Epclusa, a close monitoring of International Normalised Ratio (INR) values is recommended. Interactions between Epclusa and other medicinal products: Acid reducing agents including antacids (aluminium, magnesium hydroxide, calcium carbonate), H2-receptor antagonists (famotidine, cimetidine, nizatidine, ranitidine), proton pump inhibitors (omeprazole, lansoprazole, rabeprazole, pantoprazole, esomeprazole); Antiarrhythmics such as amiodarone, digoxin; Anticoagulants such as dabigatran etexilate and Vitamin K antagonists; Anticonvulsants such as carbamazepine, phenytoin, phenobarbital and oxcarbazepine; Antifungals such as ketoconazole, itraconazole, voriconazole, posaconazole and isavuconazole; Antimycobacterials such as rifampicin, rifabutin and rifapentine; HIV antiviral agents: reverse transcriptase inhibitors such as tenofovir disoproxil fumarate, efavirenz/ emtricitabine/ tenofovir disoproxil fumarate, sofosbuvir/ velpatasvir and emtricitabine/ rilpivirine/tenofovir disoproxil fumarate; Herbal supplements such as St. John's wort; HMG-CoA reductase inhibitors such as rosuvastatin, and statins.

Before prescribing, please consult full prescribing information which is available upon request.
Epclusa is a registered trademark of Gilead Sciences, Inc., or its related companies.

Hong Kong: For medical enquiries, please send your request to asiamedinfo@gilead.com or call 800 908 348 (toll-free number)
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18 YEARS OF SAFEGUARDING HONGKONGERS' STOMACHS[1]

Nexium™ esomeprazole 耐信™

Flexible

Administration

i. Oral[3]

ii. Intravenous[4]

Formulation[3,5]

NEXIUM™ MUPS tablets can be taken with or without food and facilitates administration for patients with difficulty swallowing

Unrivalled compare to Pantoprazole:

a. Higher percentage of time with intragastric pH>4 by 9.8% (p<0.001)[6]

b. 2 Days faster heartburn symptom relief (p<0.001)[7]

c. Superior healing rate of erosive oesophagitis by 3.5% (p<0.001)[7]

d. Superior sustained remission of erosive oesophagitis by 12.1% (p<0.0001)[8]

Unrivalled compare to Lansoprazole:

a. Higher percentage of time with intragastric pH>4 by 10.5% (p≤ 0.0001)[9]

b. 1 Day faster heartburn symptom relief (p≤0.01)[10]

c. Superior healing rate of erosive oesophagitis by 3.8% (p=0.0001)[10]

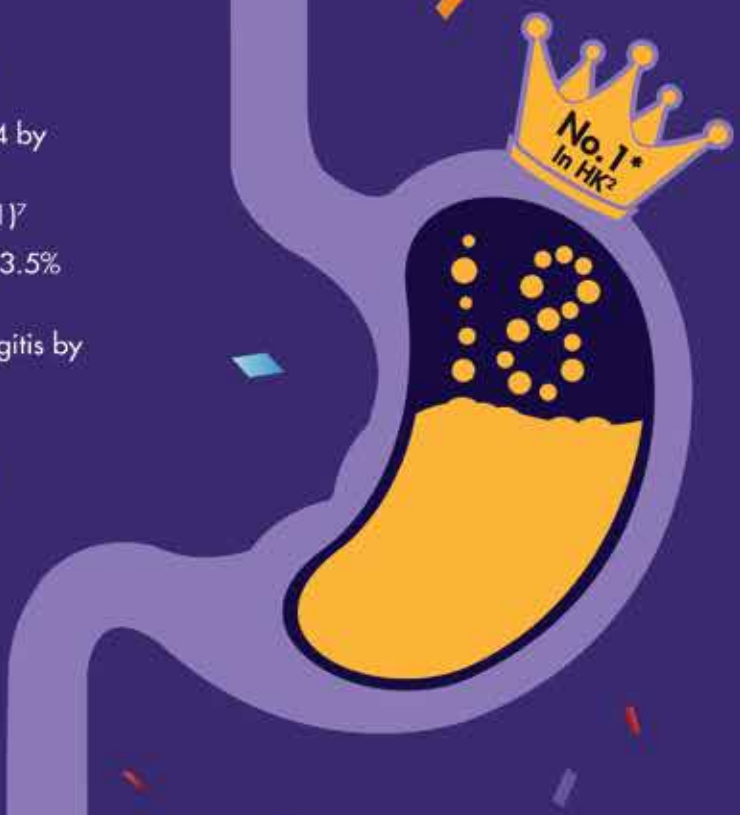
d. Superior sustained remission of reflux oesophagitis by 9% (p<0.0001)[11]

Safety of Long Term Therapy[12]

In patients with healed erosive esophagitis received Nexium™ 40 mg for up to 12 months

Treatment-related adverse events reported by >3% of patients (diarrhea, abdominal pain, flatulence, and headache only)

- No serious drug-related adverse events



References:
1. Drug Office, Department of Health. Search Drugs Database - NEXIUM TAB 20MG 2019 [cited 2019 Feb 18]. Available from: https://www.drugoffice.gov.hk/eps/drug/productDetail/en/consumer/100605. 2. IMS Data - PPI Sales Value Share. 2018. 3. NEXIUM™ Tablets. Prescribing Information. April 2016. Doc ID-002203368 v12. 4. NEXIUM™ Powder for Solution for Injection/Infusion. Prescribing Information. April 2016. Doc ID-002253657 v6. 5. Johnson DA. Review of esomeprazole in the treatment of acid disorders. Expert Opin Pharmacother. 2003;4:253-64. 6. Wilder-Smith C, Bäcklund A, Eckerwall G, Lind T, Fiellmin M, Rohss K. Effect of increasing esomeprazole and pantoprazole doses on acid control in patients with symptoms of gastro-oesophageal reflux disease: a randomized, dose-response study. Clin Drug Investig. 2008;28:333-43. 7. Labenz J, Armstrong D, Lauritsen K, Katelaris P, Schmidt S, Schutze K, et al. A randomized comparative study of esomeprazole 40 mg versus pantoprazole 40 mg for healing erosive oesophagitis: the EXPO study. Aliment Pharmacol Ther. 2005;21:739-46. 8. Labenz J, Armstrong D, Lauritsen K, Katelaris P, Schmidt S, Schutze K, et al. Esomeprazole 20 mg vs. pantoprazole 20 mg for maintenance therapy of healed erosive oesophagitis: results from the EXPO study. Aliment Pharmacol Ther. 2005;22:803-11. 9. Miner P, Jr., Katz PO, Chen Y, Sostek M. Gastric acid control with esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole: a five-way crossover study. Am J Gastroenterol. 2003;98:2616-20. 10. Castell DO, Kahrilas PJ, Richter JE, Vakil NB, Johnson DA, Zuckerman S, et al. Esomeprazole (40 mg) compared with lansoprazole (30 mg) in the treatment of erosive esophagitis. Am J Gastroenterol. 2002;97:575-83. 11. Lauritsen K, Dewint J, Rigaud MA, Boyerdorffer E, Mózsik G, Murray F, et al. Esomeprazole 20 mg and lansoprazole 15 mg in maintaining healed reflux oesophagitis. Metropole study results. Alimentary Pharmacology & Therapeutics. 2003;17:333-41. 12. Muton PN, Vakil NB, Levine JG, Hwang C, Skammer W, Lundborg P. Safety and efficacy of long term esomeprazole therapy in patients with healed erosive oesophagitis. Drug Saf. 2001;24:625-35.

More information is available upon request.

Please contact (+852) 2420 7388 or HKPatientSafety@astrazeneca.com for reporting Individual Case Safety Report (ICSR) to AstraZeneca Hong Kong Limited.

NexiumTM is a trademark of AstraZeneca group of Companies.

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AstraZeneca Hong Kong Limited
Unit 1-3, 11/F, 18 King Wah Road, North Point, Hong Kong
Tel: (852) 2420 7388 Fax: (852) 2422 6788
www.astrazeneca.com.hk