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June 2021

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President Message

Welcome to our June 2021 Newsletter!

While we are still living under the coronavirus pandemic in the midst of 2021, everyone is adapting to the many new norms in daily life in order to keep us all safe and keep things moving. The blooming of virtual meetings is a typical example. And, it is in this way, after passing the special resolution during our Extraordinary General Meeting on 18 January 2021, we had our first-ever hybrid Annual General Meeting and virtual Annual Scientific Meeting on 9 March this year. During the ASM, honorary fellowship was bestowed upon Professor Ernst J. Kuipers, Professor of Medicine, Erasmus MC University of Medical Centre, Rotterdam, The Netherlands, who also delivered his lecture to us from the other side of the globe. The 23rd Joint Annual Scientific Meeting will be held on 17 October 2021 in the format of hybrid. Please stay tuned to our website for details.

I would like to thank Dr. Wai-Fan Luk for organizing the Annual General Meeting cum Scientific Meeting on 9 March 2021, Professor Wai-Keung Leung for editing this Newsletter, Dr. Michael Ka-Shing Cheung, Dr. Joyce Wing-Yan Mak and Dr. Edmund Siu-To Wu for their scientific updates in this Newsletter. Last but not least, all the sponsors who rendered support and contributions to the Society.

The next newsletter will be published in December 2021.

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

Scientific Updates

Post-colonoscopy colorectal cancer

Dr. Michael Ka-Shing Cheung
Clinical Assistant Professor
Department of Medicine
The University of Hong Kong
Hong Kong

Overview of post-colonoscopy colorectal cancer

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer-related mortality worldwide.[1] Despite screening by colonoscopy, which reportedly reduces CRC incidence and mortality, post-colonoscopy colorectal cancer (PCCRC) can still be diagnosed months or years after a negative examination.[2] CRC diagnosed before the next recommended surveillance examination is called an interval PCCRC.[2]

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*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-TARGET2 and TRIO network[2,4]. SVR12 rate was 96.1% (294/306) in overall treatments2, and 91.5–98.1% (1398/1450 in total) across the genotypes 1–6[2,4]

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-APR20-EU-MAR20). 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 Studvy. 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 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. 4. Tsai N, et al. Utilization of DAA therapies ledipasvir/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-APR20-EU-MAR20)
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: Epclusa can be used in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2) and end stage renal disease (ESRD) requiring haemodialysis with no dose adjustment. 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 strong P-glycoprotein (P-gp) or strong cytochrome P450 (CYP) inducers (carbamazepine, phenobarbital, phenytoin, rifampicin, rifabutin and St. John's wort). 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: Life-threatening cases of severe bradycardia and heart block have been observed when sofosbuvir-containing regimens are used in combination with amiodarone. Amiodarone should only be used in patients on Epclusa when other alternative anti-arrhythmic treatments are not tolerated or are contraindicated. Patients should undergo cardiac monitoring in an in-patient setting for the first 48 hours of coadministration, after which outpatient or self-monitoring of the heart rate should occur on a daily basis through at least the first 2 weeks of treatment. 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 with concurrent or recent use of amiodarone should be warned of the symptoms of bradycardia and heart block and should be advised to seek medical advice urgently should they experience them. 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. 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: Safety data are limited in patients with severe renal impairment (eGFR < 30 mL/min/1.73 m^2) and ESRD requiring haemodialysis. Epclusa can be used in these patients with no dose adjustment when no other relevant treatment options are available. 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. efavirenz, modafinil, oxcarbazepine or rifapentine) 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. Use in diabetic patients: Diabetics may experience improved glucose control, potentially resulting in symptomatic hypoglycaemia, after initiating HCV direct-acting antiviral treatment. Glucose levels of diabetic patients initiating direct-acting antiviral therapy should be closely monitored, particularly within the first 3 months, and their diabetic medication modified when necessary. The physician in charge of the diabetic care of the patient should be informed when direct-acting antiviral therapy is initiated. 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-containing regimens are used in combination with amiodarone and/or other medicinal products that lower heart rate. Steven-Johnson syndrome with unknown frequency. **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. Impact of DAA therapy on drugs metabolized by the liver: The pharmacokinetics of drugs that are metabolized by the liver (e.g. immunosuppressive agents such as calcineurin inhibitors) may be impacted by changes in liver function during DAA therapy, related to clearance of HCV. Interactions between Epclusa and other medicinal products: Acid reducing agents including antacids (aluminium, magnesium hydroxide, calcium carbonate), H_2-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; Antimycobacterials such as rifampicin, rifabutin and rifapentine; HIV antiviral agents: reverse transcriptase inhibitors such as tenofovir disoproxil fumarate, efavirenz/ emtricitabine/ tenofovir disoproxil fumarate; Herbal supplements such as St. John's wort; HMG-CoA reductase inhibitors such as rosuvastatin, and other statins. Immunosuppressants such as ciclosporin and tacrolimus.

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Interval PCCRC accounts for approximately 2–9% of all CRCs.[3] A meta-analysis of 12 studies showed that the prevalence of interval PCCRC declined from 4.8% in 1990s to 3.7% beyond 2005, and this cancer was 2.4 times more likely to arise in the proximal colon than the distal colon (6.5% vs 2.9%).[4]

Characteristics of interval PCCRC differ from those of detected CRC

Compared with patients with detected CRC, patients diagnosed with interval PCCRC are more likely to be older, have a family history of CRC, have been diagnosed with colonic diverticulosis, have undergone polypectomy on their index colonoscopy and have had their index colonoscopy performed by a non-gastroenterologist.[4]

Interval PCCRCs are more likely to be CpG island methylator phenotype (CIMP)-positive and microsatellite instability-high (MSI-H) than detected CRCs. Furthermore, they are less likely to be diagnosed at an advanced stage and have a better prognosis, with a 37% lower risk of mortality than detected CRCs.[4]

Risk factors for interval PCCRC development and measures to reduce incidence

Common causes of interval PCCRC development include missed lesions (~60% of cases), incompletely resected lesions (~20%) and new lesions (~25%).[3]

Missed lesions

A meta-analysis of 43 publications showed miss rates of 26% for adenomas and 9% for advanced adenomas in 15,152 index diagnostic colonoscopies. Miss rates were high for proximal advanced adenomas (14%), serrated polyps (27%) and flat adenomas (34%).[5] A large multicentre study (n=294) found that the diameter (1-mm increments) was associated with a lower miss rate, whereas sessile- or flat-shaped polyps were associated with a higher miss rate.[6]

Professional societies recommend adenoma detection rates (ADRs), defined as the proportion of patients with one or more adenomas detected during screening colonoscopy, of at least 25% in asymptomatic, average-risk individuals aged ≥50 years (≥30% for men and ≥20% for women) as indicators of adequate colonoscopy quality.[7] Evidence suggests that the risk of interval PCCRC decreases linearly with increasing ADRs; each 1% increase in ADR is associated with 3% and 5% reductions in the risk of interval PCCRC incidence and mortality, respectively.[8]

Endoscopist characteristics influence the likelihood of missing a lesion. Patients whose colonoscopies were performed by a gastroenterologist or general surgeon, or by an endoscopist with a high completion rate or one who performed high rates of polypectomies, were less likely to develop a PCCRC.[9]

A study of 7,882 colonoscopies performed by 12 experienced gastroenterologists revealed a linear correlation between ADR and colonoscopic withdrawal time. Colonoscopists with a mean withdrawal time of ≥6 minutes had higher ADRs than those with a mean withdrawal time of <6 minutes.[10]

Inadequate bowel preparation for colonoscopy may hinder detection of smaller lesions (≤9 mm).[11] Splitting the large volume of polyethylene glycol (PEG) solution was shown to improve the quality of bowel preparation, leading to a more thorough examination of the mucosa and fewer missed lesions, compared with full PEG dosing.[12]

The use of narrow-band imaging was found to detect more adenomas, non-adenomatous polyps and flat polyps than white-light endoscopy, and the effect was greater when bowel preparation was optimal.[13]

Lesions can be missed particularly if they are located behind folds and flexures in the colon. The Third Eye Retroscope device has been shown to increase ADR during colonoscopy by providing a retrograde view that complements the colonoscope's forward view.[14]

In addition, incorporating artificial intelligence with real-time computer-aided polyp detection significantly increased ADR (risk ratio 1.44; $p<0.01$) compared with control, according to a meta-analysis of five randomized controlled trials (n=4,354).[15]

Incompletely resected lesions

The prospective CARE study, involving 1,427 patients with 346 neoplastic polyps removed during colonoscopies, revealed that about 10% of the polyps were incompletely resected. Incomplete resection rate was significantly higher for large (10–20 mm) than small (5–9 mm) neoplastic polyps (17.3% vs 6.8%; $p=0.003$) and for sessile serrated adenomas/polyps than for conventional adenomas (31.0% vs 7.2%; $p<0.001$).[16]

Magnification endoscopy helps detect residual adenomatous tissue in case of piecemeal resection of large sessile polyp.[17] Applying argon plasma coagulation to the edge and base of the polypectomy site may also help reduce adenomatous recurrence after resection.[18]

Surveillance interval recommendation

The goals of colonoscopy screening and surveillance are to reduce CRC incidence and mortality. The United States Multi-Society Task Force recently updated their recommendations on the interval for surveillance colonoscopy based on stratification of risk for metachronous advanced neoplasia (Figure).[19] The European Society of Gastrointestinal Endoscopy also proposed a similar guideline but it is simplified to having surveillance intervals at 3, 5 or 10 years.[20]

Some medications may have chemoprotective effects

Although aspirin may reduce CRC risk,[21] it was not found to be associated with a lower risk of PCCRC development, according to a retrospective cohort study (n=187,897) based on a territory-wide healthcare database in Hong Kong. Instead, non-steroidal anti-inflammatory drugs (NSAIDs) demonstrated a 46% reduction in the 3-year PCCRC risk (defined as cancer diagnosed 6–36 months after index colonoscopy).[22] Statin use was also associated with a 38% reduction in the 3-year PCCRC risk.[23]

Conclusion

Interval PCCRC can occur before the next recommended surveillance examination after an initial colonoscopy negative for CRC. Missed lesions, incomplete polypectomy and new CRCs are the main sources of PCCRC cases, and these factors can be targeted to reduce the risk of PCCRC. Certain medications may have protective effects against CRC development according to observational studies, but further investigations are needed to confirm their benefits.

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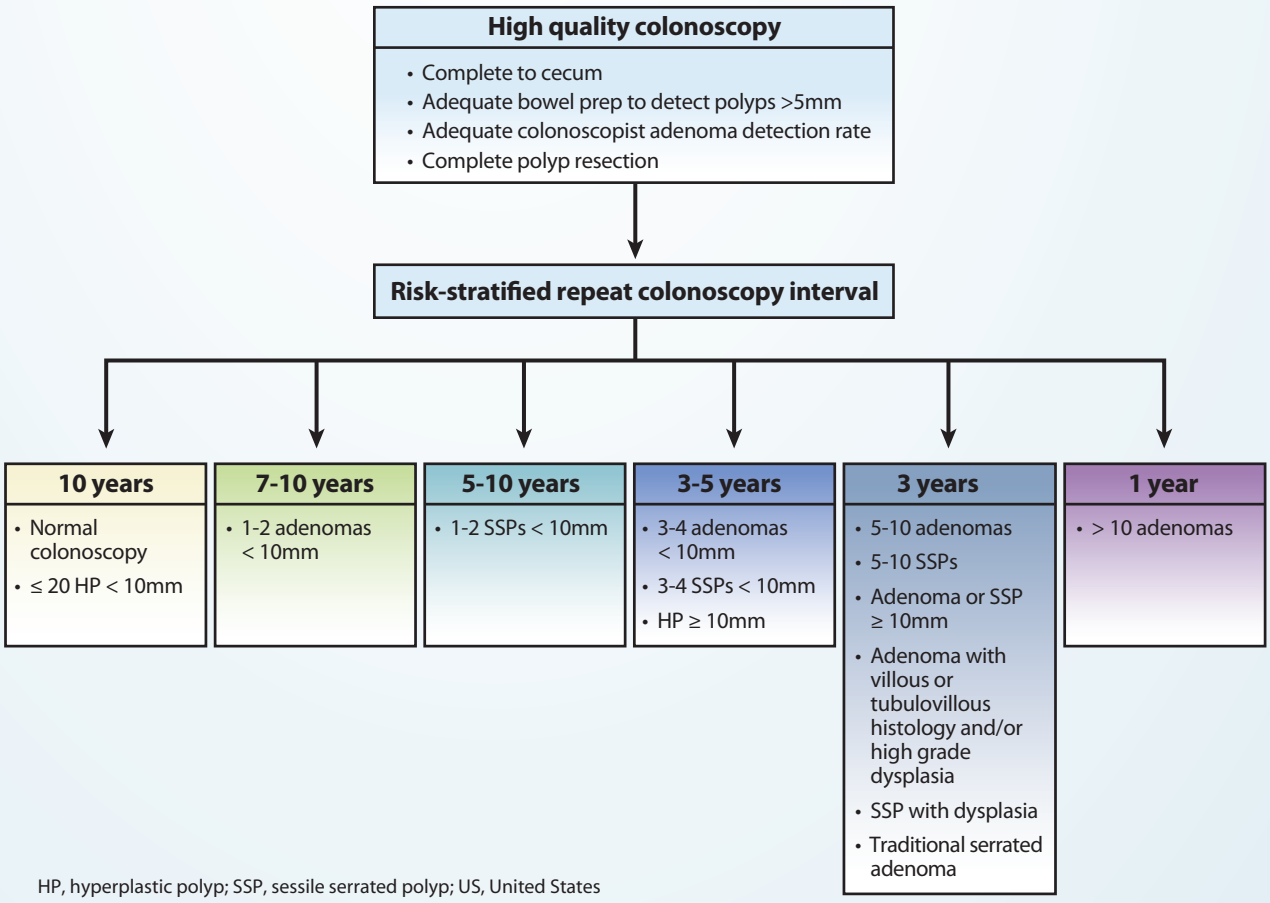
Figure. The US Multi-Society Task Force recommendations for follow-up after colonoscopy and polypectomy[19]



HP, hyperplastic polyp; SSP, sessile serrated polyp; US, United States

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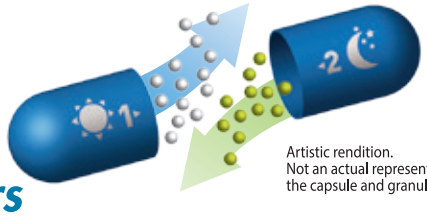

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C-APROM/HK/DEXI/0011 (02/2021)

Update on the management of perianal Crohn's disease

Dr. Joyce Wing-Yan Mak
Assistant Professor
Department of Medicine and Therapeutics
The Chinese University of Hong Kong
Hong Kong

Perianal Crohn's disease: A distinct, aggressive and disabling phenotype of Crohn's disease

Perianal Crohn's disease (PCD) affects one-third of patients with Crohn's disease (CD). The presence of PCD at initial presentation is associated with an increased number of hospital admissions and surgical resections in the subsequent 5 years and predisposes patients to chronic disabling symptoms and causes significant morbidity.[1]

PCD is more prevalent in the Asian population than in Caucasians and in those who are young, male and with a penetrating phenotype of CD.[1,2] Data from the Hong Kong territory-wide inflammatory bowel disease (IBD) registry revealed that 29% of patients with CD (n=981) had perianal involvement, of which 42% had PCD diagnosed at first presentation. The majority of patients with PCD were male (79%) and the mean age at diagnosis was 29 years.[1]

Combined surgical and medical treatment results in better patient outcomes

Surgical treatment of PCD

Surgical treatment usually involves examination under anaesthesia (EUA), abscess draining and/or seton insertion, and the goals are to control sepsis before initiating medical treatment, achieve fistula closure, relieve symptoms and preserve sphincter function.[3]

Video-assisted anal fistula treatment (VAAFT) is a sphincter-sparing, minimally invasive technique that allows viewing of the fistula from the inside so that it can be eradicated under direct vision using a fistuloscope. A study of VAAFT in 25 patients with complex Crohn's perianal fistula demonstrated an improvement in patient-reported outcomes in terms of pain and discharge scores in 84% of patients.[4]

The Fistula Laser Closing (FiLaC™) device is another endo-fistular management technique that uses a radial probe to cause denaturation and scarring along the fistula with obliteration of the internal and external fistula orifices. A study that assessed healing success with FiLaC in a cohort of patients with Crohn's-related fistulae (n=117) showed that 69% (9/13) of patients maintained complete fistula closure at 5 years.[5]

Temporary faecal diversion (FD) of the faecal stream is sometimes used to control the inflammatory burden, along with concomitant medical therapy, to improve quality of life and avoid proctectomy. However, a meta-analysis showed that restoration of bowel continuity was successful in only a small proportion of patients and nearly half of them required proctectomy after failure of temporary FD.[6]

Medical treatment

Pre-biologic era with antibiotics and thiopurines

Metronidazole and ciprofloxacin are antibiotics commonly used in the first-line management of PCD and infectious complications.[7] A head-to-head comparison of metronidazole and ciprofloxacin in a small randomized controlled trial (n=25) showed no statistically significant differences between the two treatments in terms of response or remission rates in patients with actively draining perianal fistulas.[8] About 60% of patients achieved a clinical response to the combination of metronidazole and ciprofloxacin within 12 weeks but the response was not durable.[7]

In a meta-analysis of five studies (n=70), more patients with active CD demonstrated clinical fistulae response with thiopurines (azathioprine or 6-mercaptopurine) than with placebo (54% vs 21%), with an overall odds ratio of 4.44 (95% confidence interval 1.5–13.2) favouring thiopurines.[9]

Treatment with biologics

Anti-tumour necrosis factor (TNF) agents have shown effectiveness in fistula healing and improve quality of life in patients with PCD.[10] In the randomized, double-blind ACCENT II trial (n=306), more patients with perianal fistulas who received infliximab as maintenance therapy had a clinical response at 54 weeks compared with placebo (46% vs 23%; p=0.001), and infliximab reduced the rates of hospitalizations, surgeries and procedures compared with placebo.[11,12]

Adalimumab demonstrated effectiveness in anti-TNF-naive or -refractory patients with active CD in the phase IIIb, open-label CHOICE trial (n=673). Complete fistula healing was achieved in 39% of patients with baseline fistulas.[13]

Combining anti-TNF treatment with surgery resulted in improved patient outcomes. A retrospective study of patients with PCD (n=32) found that patients who had surgical EUA and seton placement before infliximab had a better initial response rate and a lower recurrence rate than patients who received infliximab alone (Figure).[14] Yassin and coworkers[15] also reported beneficial effects of combination therapy on fistula healing in patients with PCD compared with surgery or medical therapy alone, based on a systematic review of 24 articles.

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1 Bar-Meir et al. Dis Colon Rectum. 2003; 46(7): 929 – 36.
2 Gross et al. Aliment Pharmacol Ther. 2006; 23(2): 303 – 12.

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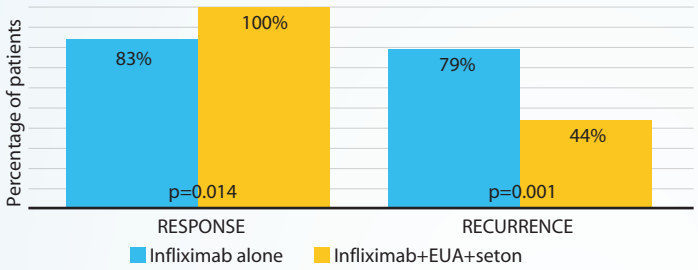
Figure. Rates of initial response and recurrence in patients with PCD treated with infliximab with or without prior surgery[14]



EUA, examination under anaesthesia; PCD, perianal Crohn's disease
Response was defined as complete closure and cessation of drainage from the fistula.

Notably, high infliximab trough levels during induction are associated with favourable fistula response to anti-TNF treatment. A retrospective, observational cohort study (n=36) found that infliximab levels of 9.25 µg/mL at Week 2 and 7.25 µg/mL at Week 6 were the best predictors of fistula response.[16]

Vedolizumab and ustekinumab are other potentially effective biologic options for PCD.[17] Mesenchymal stem cell therapy also successfully induced clinical remission in patients with PCD in a phase III study.[18] However, a meta-analysis of 27 controlled trials found that anti-TNF agents were the only biologics with robust evidence of effectiveness for both induction and maintenance of perianal fistula response and remission.[17]

Maintenance therapy with biologics may prevent relapse

Radiological healing can lag behind clinical remission by a median of 12 months.[19] Radiologically healed fistula tracts maintain healing but more than half of patients with PCD experience relapse after cessation of anti-TNF therapy.[20] Using data from prospective IBD databases (n=78), the cumulative probabilities of PCD relapse at 1 year and 3 years were estimated at 51% and 73%, respectively, in the Asian population. Among patients with PCD relapse, 83% achieved remission when re-treated with anti-TNF therapy; 27% required defunctioning surgery and 2% required proctectomy.[21]

In a retrospective study of 20 patients with PCD, the mean duration from diagnosis to radiological healing was 68 months, and two-thirds of patients who stopped biologic therapy (n=9) went on to develop fistula relapse, with median time to recurrence of 21 months. These findings suggest that radiological healing may not be an appropriate marker for ceasing biologic therapy.[22]

Conclusion

Anti-TNF agents have the best evidence for successful fistula healing to date, but a multidisciplinary approach, including medical and surgical therapy with radiological guidance, should be the gold standard for the management of PCD. However, further studies are needed to optimize close monitoring and guide possible treatment withdrawal strategies.

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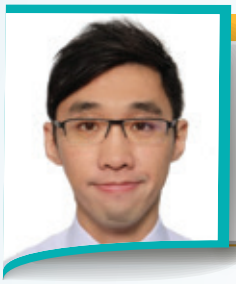
Rectal Sucralfate Gel Treatment in Patients with Chronic Radiation Proctitis – A Pilot Study in a Regional Hospital in Hong Kong (Summary of Thesis 2020)



Dr. Edmund Siu-To Wu
Department of Medicine and Geriatrics,
Princess Margaret Hospital
Hong Kong

Introduction

Radiation proctitis is a common complication of radiotherapy for pelvic malignancies. Acute radiation proctitis occurs up to three months after radiotherapy and is usually self-limited. In contrast, chronic radiation proctitis occurs either after three months of radiotherapy or as progression from acute phase.[1] Chronic radiation proctitis is a syndrome marked by rectal bleeding, tenesmus, fecal incontinence, and mucus discharge.[2] Its endoscopic findings include mucosal friability, telangiectasia, ulcerations, fistulas, and strictures.

Radiation proctitis is reported in up to 20% of patients who undergo pelvic radiotherapy.[3] A retrospective study on prostate cancer patients who received radiotherapy in Hong Kong showed that rates of late rectal toxicities were 46.5%.[4] Management of chronic radiation proctitis is challenging. Experience is mostly derived from case reports, and small clinical trials. There are medical, endoscopic and surgical therapies, but the results can be disappointing.[2]

Sucralfate is an aluminum salt of sucrose octasulfate which is used in peptic ulcer disease. It adheres to mucosa, protects intestinal lining, stimulates prostaglandin synthesis, and increases local blood flow and epidermal growth factor production.[5,6] A small randomized controlled trial conducted by Kochhar et al in 1991 comparing sucralfate enema (17 patients) versus prednisolone enema plus oral sulfasalazine (15 patients) in radiation proctosigmoiditis demonstrated clinical improvement in 94% and 53% patients respectively.[7]

The best form for rectal sucralfate has yet to be determined. Previously, sucralfate enema was prepared by suspending powdered sucralfate tablets in water. Compared to sucralfate non-gel preparations, sucralfate gel is demonstrated to persist longer in gastrointestinal tract, and have better mucoadhesion and resistance to removal.[8,9] Therefore, sucralfate gel can be an effective form of rectal sucralfate for treatment of chronic radiation proctitis.

This prospective pilot study is the first trial in Hong Kong to evaluate the efficacy and safety of sucralfate rectal enema prepared from sucralfate oral gel for treatment of chronic radiation proctitis, introduce the method of sucralfate gel enema administration, and assess treatment compliance in a Chinese patient population.

Methods

This single-centered prospective study included 25 patients with symptomatic chronic radiation proctitis between 2019 and 2020. Patients were excluded if they had acute radiation proctitis, other proctitis or end stage renal disease. Each patient received two grams twice-daily sucralfate gel enema for 8 weeks, and were followed up for 24 weeks. Sucralfate gel enema was prepared by mixing 10 mL (two grams) of sucralfate gel with 10 mL of warm water, drawn up with 25 mL syringe, and administered through a 16-French catheter inserted 5-8 cm into anal verge. Patients were instructed to retain rectal enema in four positions every 3-5 minutes: left lateral, supine, right lateral, and prone positions. Method to administer sucralfate gel enema was explained to patients and/or family. Initial enema administration was observed in hospital to ensure safe delivery. Written instructions with photo illustrations were provided.

Clinical symptoms were graded by Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 by U.S. National Cancer Institute.[10] Endoscopic findings were scored by Vienna Rectoscopy Score (VRS).[11] Each patient underwent flexible sigmoidoscopy before and after treatment. Hemoglobin level and iron profiles were taken before and after treatment. Statistical analysis was performed with IBM SPSS Statistics version 26.0.

Results

Demographics

Mean patient age was 70.7 years. 76% patients were male. 96% patients were Chinese, and one was Caucasian. 72% patients had prostate cancer, 24% had cervical cancer, and 4% had rectal cancer. Mean radiation dosage was 73.9 Gy. Onset of symptoms occurred at mean of 8.9 months after radiotherapy. 20% patients were on anti-platelet agents, and 8% were on anticoagulants. Some patients had previous treatments: 72% had used prednisolone enema, 40% had argon plasma coagulation, and 4% had hyperbaric oxygen treatment, topical formalin and mesalazine suppository. 36% patients were on iron replacement. 28% patients had history of average 5.7 units blood transfusion for radiation proctitis. No patient had sucralfate enema before.

Clinical Symptoms

100% patients presented with rectal bleeding, one patient with diarrhea, one with rectal pain, and one with fecal incontinence. CTCAE Grade for rectal bleeding had significantly improved over time during 24-week study period ($P<0.001$). Mean CTCAE Grade of rectal bleeding was 2.16 at baseline. It had significantly improved to 1.16 at week 4, 1.08 at week 8, 0.96 at week 16, and 0.92 at week 24 ($P<0.001$) **(Table 1)**.

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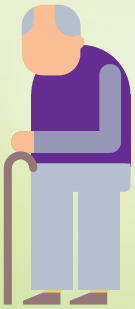

Chronic diseases*,3

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≥2 diseases: 40.5% (458,600 persons)

Diabetes*,3

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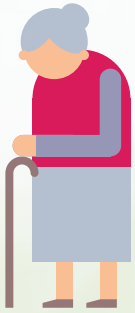

Chronic medications*,3

1-4 medications: 57.2% (30,900 persons)

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* Based on the data from the 2009 survey on health status and self-care capability of older persons (age ≥60 years) residing in domestic households and residential care institutions in Hong Kong[3].

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Table 1. Mean CTCAE Grades for Rectal Bleeding at Week 0, 4, 8, 16 and 24.

	Mean ± SD	Change from Week 0	P[a]
Week 0	2.16 ± 0.62	–	–
Week 4	1.16 ± 0.94	-1.00 ± 0.82	<0.001
Week 8	1.08 ± 0.91	-1.08 ± 0.86	<0.001
Week 16	0.96 ± 0.89	-1.2 ± 0.87	<0.001
Week 24	0.92 ± 0.91	-1.2 ± 0.93	<0.001

[a] Wilcoxon signed-rank test comparing CTCAE from Week 0.

Before sucralfate gel enema, 28% patients had CTCAE Grade of 3, 60% had CTCAE of 2, and 12% had CTCAE of 1 for rectal bleeding. After enema at week 24, 8% patients had CTCAE of 3, 12% had CTCAE of 2, 44% had CTCAE of 1, and 36% had CTCAE of 0 for rectal bleeding **(Table 2)**.

Table 2. CTCAE Grades for Rectal Bleeding before treatment and at Week 24.

Grade	Before treatment, n	Week 24, n
0	0	9
1	3	11
2	15	3
3	7	2
4	0	0
5	0	0

Rectal sucralfate gel achieved improvement in CTCAE Grade for rectal bleeding in 72% patients at week 4 and week 8, 84% patients at week 16, and 88% patients at week 24. Only 3 (12%) patients did not respond to sucralfate gel enema by week 24, for which 1 of them had worsening CTCAE from Grade 2 to 3. 36% patients at week 24 had resolution of rectal bleeding. 16% patients required blood transfusion, and 8% patients required additional iron supplementation during 24-week study period.

Before sucralfate gel enema, one patient had diarrhea with CTCAE score of one, and one had rectal pain with CTCAE score of one. Both patients had resolution of diarrhea and rectal pain after treatment. One patient, 77 years old man, had fecal incontinence, with the same CTCAE score of two before and after treatment.

Endoscopic findings

Mean score of VRS was 2.6 before treatment and 2.5 after treatment. There was no significant difference in VRS before and after treatment (P=0.083).

Laboratory data

There was no significant difference in hemoglobin (P=0.121), iron (P=0.439), iron saturation (P=0.113), and ferritin (P=0.112) before and after treatment.

Adverse event

There was no severe adverse event related to sucralfate gel enema. 52% patients reported mild symptoms after enema, in which 40% had bowel urgency and 16% had lower abdominal bloating.

Compliance and drug administration

84% patients were compliant with 20 mL sucralfate gel enema twice-daily regimen. 76% patients were able to administer enema themselves, and 24% had their partners administered it.

Discussion

This study showed that severity of rectal bleeding had significantly improved after 8 weeks of sucralfate gel enema over 24-week study period. Sucralfate gel enema achieved improvement in rectal bleeding in 72% patients at week 4 and 8, 84% patients at week 16, and 88% patients at week 24 in terms of CTCAE Grades. This was comparable to the result of Kochhar et al study in 1999, where rectal sucralfate showed good responses in 76.9% patients at 4 weeks, 84.6% patients at 8 weeks, and 92.3% patients at 16 weeks.[12] In our study, 36% patients at week 24 had resolution of rectal bleeding. Rectal pain and diarrhea were resolved in the two patients. No patient developed severe adverse event. This study demonstrated that sucralfate gel enema could be a promising treatment of chronic radiation proctitis.

There was no significant difference in endoscopic VRS before and after sucralfate gel enema. It is probably because the VRS system[11] weighs heavily on the severity of telangiectasia, which are less likely to improve in a short time period.

In this study, 84% patients were compliant with twice-daily sucralfate gel enema regimen. 76% patients with mean age of 69.6 years were able to self-administer sucralfate enema, and another six patients with mean age of 74.2 years were able to have their elderly partners administered enema for them. Elderly people can administer rectal enema, provided that clear oral and written instructions are given. In contrast to conventional thinking that elderly Chinese patients are reluctant to use rectal enema, this study shows encouraging result that even elderly Chinese population can be compliant with and competent in administering sucralfate gel enema.

Although no patient developed severe adverse event, 52% patients reported mild symptoms such as bowel urgency and lower abdominal bloating after enema. These mild symptoms could be related to the nature of rectal enema. Prednisolone enemas prescribed at our institute are of volumes of 100 mL. In contrast, sucralfate gel enema has a much smaller volume of 20 mL, thus minimizes patient discomfort. In addition, patients reported that it was easier and more comfortable to use the soft and long catheter in sucralfate enema administration than the hard and short nozzle in prednisolone enema administration.

The study has its limitation in terms of sample size and duration of treatment and follow up. Clinical oncology service in our hospital serves the entire Kowloon West Cluster. Future study will need to recruit more patients from other clusters of Hospital Authority. In addition, the study will need to have longer treatment and follow up duration in order to detect significant differences in endoscopic scores and laboratory results.

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Conclusion

Sucralfate gel enema can be an effective treatment for chronic radiation proctitis. It can be safely administered by elderly Chinese patients and with satisfactory compliance rate. The positive clinical outcome in this initial experience of sucralfate gel enema provides the basis for future randomized controlled trial.

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40th Annual General Meeting cum Scientific Meeting of The Hong Kong Society of Gastroenterology

Date: 9 March 2021

Format: Online Zoom

Organizing Chairperson: Dr. Wai-Fan Luk

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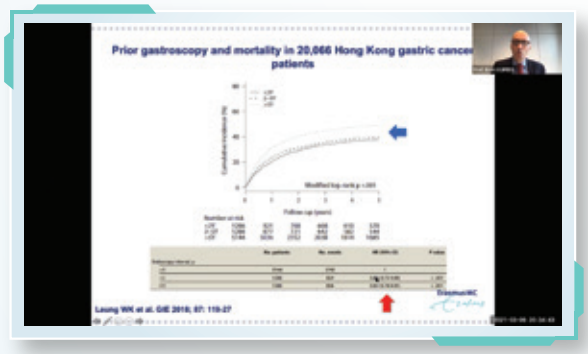
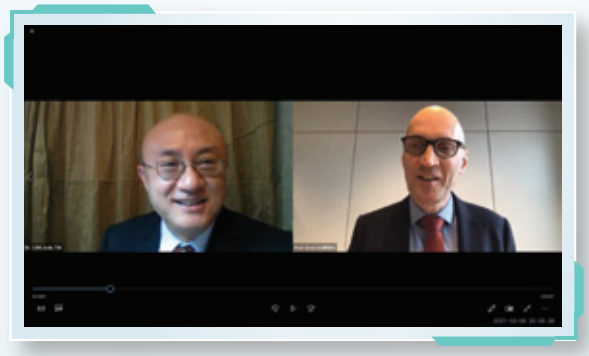
Due to COVID-19 pandemic, the Society's first-ever virtual Annual General Meeting cum Scientific Meeting was held on 9 March this year. The annual general meeting was attended by 34 fellows and members during which the Society's annual report and financial statements for the year 2020 were presented. Seven fellows were elected to the Council for the term of 2021-2023.

The annual scientific meeting then followed was attended by 175 healthcare professionals. The honorary fellowship of our Society was bestowed upon distinguished guest, Professor Ernst J. Kuipers, Professor of Medicine, Department of Gastroenterology & Hepatology, Erasmus MC University Medical Centre, Rotterdam, The Netherlands. He is among the 23 honorary fellows of our Society who are renowned scholars in the specialty.

Professor Kuipers delivered an enlightening lecture on "Surveillance of gastric intestinal metaplasia finally coming of age". It was followed by "Double-balloon enteroscopy assisted ERCP for patients with surgically altered anatomy" presented by Dr. Ka-Shing Cheng. The panel discussion led by Dr. David Y.K. But, Dr. Kenneth S.H. Chok and Dr. Yuk-Tong Lee was well-received.





Online Joint Scientific Symposium
COVID-19 Vaccination in IBD: Immunity and Efficacy

Date: 9 April 2021

Co-organized by: Gastroenterological Society of Singapore

Sponsor: Ferring Pharmaceuticals Limited

Topics	Speakers
Revisiting IBD Management in COVID-19: What's New?	Dr. Juanda Leo Hartono *National University of Hospital, Singapore*
Vaccinating IBD Patients	Professor Ivan Hung *University of Hong Kong, Hong Kong*
COVID-19 Vaccine: What Gastroenterologists Need to Know	Professor David M. Allen *National University Health System, Singapore*

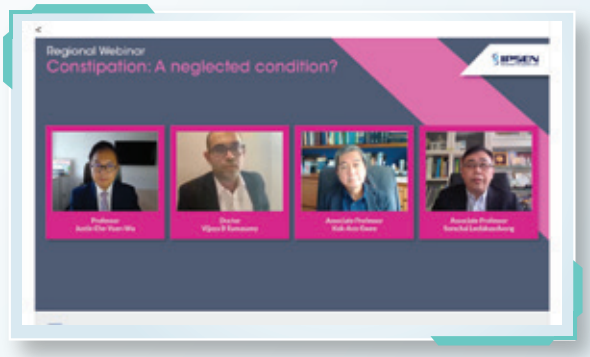
The symposium was attended by 35 local GI specialists, surgeons and healthcare professionals.

Online Scientific Symposium
Constipation: A neglected condition?

Date: 24 April 2021

Sponsor: IPSEN Pharma

Supported by: DCH Auriga (Hong Kong) Limited



Chairperson & Moderator: Dr. Vijaya B. Ramasamy
Consultant Nephrologist & Physician,
Lam Wah Ee Hospital, Malaysia

Speaker: Professor Justin Wu
Chief Operating Officer, CUHK Medical Centre
Professor, Department of Medicine, The Chinese University of Hong Kong

Panelists: Professor Justin Wu

Dr. Kok-Ann Gwee
Adjunct Associate Professor Medicine, National University of Singapore, Singapore
Consultant Gastroenterologist, Gleneagles Hospital Singapore

Dr. Somchai Leelakusolvong
Associate Professor of Medicine, Siriraj Hospital, Mahidol University, Thailand

The symposium was attended by approximately 600 healthcare professionals including about 130 local healthcare professionals.

Welcome! New Honorary Fellow

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

Coming Soon

23rd JOINT ANNUAL SCIENTIFIC MEETING 2021 (Hybrid)
Sunday, 17 October 2021

Date: Sunday, 17 October 2021

Venue: Shanghai Room, Level 8
Cordis, Hong Kong
555 Shanghai Street, Mongkok
Kowloon, Hong Kong

Organizing Chairperson: Professor Justin C.Y. Wu

Scientific Chairpersons: Dr. Thomas S.T. Lai, Dr. Tony W.C. Mak

Co-organizers:
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
Hong Kong IBD Society

Topics	Speakers
Clinical Application of Risk Scores to Predict Hepatocellular Carcinoma in Patients with Chronic Hepatitis B	Dr. Yao-Chun Hsu (Taiwan)
Risk of Surgery in patients with COVID-19	Dr. Aneel Bhangu (UK)
NAFLD	Prof. Vincent W.S. Wong (CUHK)
What's new in Chicago Classification 4.0	Prof. Justin C.Y. Wu (CUHK)
Vaccinations for IBD patients	Prof. Wai-Keung Leung (HKU)
The use of AI in GI endoscopy	Dr. Shannon Melissa Chan (CUHK)

Major Meetings

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, 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/

23-26 June 2021
EASL - The International Liver Congress 2021 - Online
Organizer: European Association for the Study of the Liver
Website: easl.eu/event/the-international-liver-congress-2021-2/

24-26 June 2021
The International Digestive Endoscopy Network (IDEN) 2021 (Hybrid)
Organizer: International Digestive Endoscopy Network
Location: Seoul, Korea
Website: www.iden.or.kr/

25-26 June 2021
International Workshop on Diagnostic and Therapeutic Endoscopy (EndoSwiss 2021- Virtual Live)
Location: Zurich, Switzerland
Website: http://www.endoswiss.ch/

2-3 & 8-10 July 2021
16th Congress of European Crohn's and Colitis Organisation (ECCO) – Virtual (ECCO 2021)
Organizer: European Crohn's and Colitis Organisation
Website: www.ecco-ibd.eu/ecco21.html

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/

2-4 July 2021
Tokyo International Endoscopy Live Seminar 2021 - Virtual
Organizer: Japan Gastroenterological Endoscopy Society
Website: www.coac.jp/tokyolive/english/

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

11-12 September 2021
Multi-specialty Medical Mega Conference 2021 (Hybrid)
Organizer: Association of Private Medical Specialists of Hong Kong
Location: Cordis, Hong Kong at Langham Place, Hong Kong
Website: www.mmmc.hk

27-30 September 2021
17th ISDE World Congress for Esophageal Diseases - Virtual
Organized by: The International Society for Diseases of the Esophagus
Website: www.isde.net

19-22 August 2021
Asian Pacific Digestive Week (APDW 2021) (Virtual)
Organizers: 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), 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 (Virtual)
Hosted by: Indonesian Hepato-Pancreato-Biliary Association, Asian-Pacific Hepato-Pancreato-Biliary Association
Location: Bali, Indonesia
Website: https://aphpba2021.com/

24-26 September 2021
Taiwan Digestive Disease Week 2021
Organizer: The Gastroenterological Society of Taiwan
Location: Taipei, Taiwan
Website: www.tddw.org/

30 September – 2 October 2021
Korea International Gastric Cancer Week 2021 – Virtual (KINGCA Week 2021)
Organizer: Korean Gastric Cancer Association
Website: www.kingca.org/html/

2-6 October 2021
29th UEG Week (Virtual)
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/

22-27 October 2021
ACG 2021 Annual Scientific Meeting and Postgraduate Course - Hybrid
Organizer: American College of Gastroenterology (ACG)
Website: http://acgmeetings.gi.org/

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

12-15 November 2021
AASLD The Liver Meeting 2021
Organizer: American Association for the Study of Liver Diseases (AASLD)
Location: California, USA
Website: www.aasld.org/event/liver-meeting

24-27 November 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/

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/

5-6 December 2021
APASL Single Topic Conference on Elimination of Hepatitis C
Organizers: Asian Pacific Association for the Study of the Liver, Myanmar GI & Liver Foundation
Location: Myanmar
Website: apaslstc2020yangon.com

9-11 December 2021
Gastro 2020 Prague
Organizers: World Gastroenterology Organisation (WGO), the Czech Society of Gastroenterology
Location: Prague, Czech Republic
Website: www.gastro2021prague.org

30 March - 3 April 2022
The 31st Conference of the Asian Pacific Association for the Study of the Liver (APASL 2022)
Organizer: The Asian Pacific Association for the Study of the Liver
Location: Seoul, Korea
Website: apasl2022seoul.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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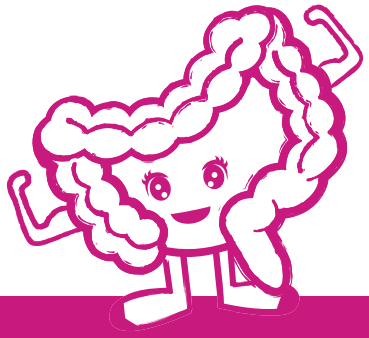
forlax® is indicated for the symptomatic treatment of constipation in adults and children aged 8 years and above.[1]



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Reference: 1/ Forlax 10g. Summary of Product Characteristics 2/ Herve S, Leroi AM, Mathiex-Fortunet H, et al. Effects of polyethylene glycol 4000 on 24-h manometric recordings of left colonic motor activity. European Journal of Gastroenterology & Hepatology. 2001 Jun; 13(6):647-54.

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Vemlidy®
tenofovir alafenamide 25mg tablets

ALT = alanine transaminase
TDF = tenofovir disoproxil fumarate
TAF = tenofovir alafenamide

The image is shown for illustration purpose only, it does not represent the actual size of the sales pack.

Reference: 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 Study 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.

VEMLIDY® Abbreviated Prescribing Information (Version: HK-FEB19-US-FEB19)
Presentation: Tablets: 25 mg of tenofovir alafenamide - yellow, round, film-coated tablets, debossed with "GSI" on one side of the tablet and "25" on the other side.

Indications: VEMLIDY is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease.

Dosage: Prior to initiation of VEMLIDY, patients should be tested for HIV-1 infection. VEMLIDY alone should not be used in patients with HIV infection. Adults: The recommended dosage is 25 mg (one tablet) taken orally once daily with food. Patients with Renal Impairment: No dosage adjustment is required in patients with estimated creatinine clearance greater than or equal to 15 mL/min, or in patients with end stage renal disease (ESRD; estimated creatinine clearance below 15 mL/min) who are receiving chronic hemodialysis. On days of hemodialysis, administer VEMLIDY after completion of hemodialysis treatment. VEMLIDY is not recommended in patients with ESRD who are not receiving chronic hemodialysis. Patients with Hepatic Impairment: No dosage adjustment is required in patients with mild hepatic impairment (Child-Pugh A). Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment.

Contraindications: None.

Warnings and Precautions: Severe acute exacerbation of Hepatitis B after discontinuation of treatment: Discontinuation of VEMLIDY, may result in severe acute exacerbations of hepatitis B. Patients who discontinue VEMLIDY should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, resumption of anti-hepatitis B therapy may be warranted. Risk of development of HIV-1 resistance in patients coinfected with HBV and HIV-1: Due to the risk of development of HIV-1 resistance, VEMLIDY alone is not recommended for the treatment of HIV-1 infection. The safety and efficacy have not been established in patients coinfected with HBV and HIV-1. HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with VEMLIDY, and, if positive, an appropriate antiretroviral combination regimen that is recommended for patients coinfected with HIV-1 should be used. New onset or worsening renal Impairment: Prior to or when initiating VEMLIDY, and during treatment with VEMLIDY on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus. Discontinue VEMLIDY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Lactic acidosis/severe hepatomegaly with steatosis: Treatment with VEMLIDY should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Adverse reactions: Refer to warning and precautions for severe acute exacerbation of hepatitis B, new onset or worsening of renal impairment, and lactic acidosis/severe hepatomegaly with steatosis. Headache, abdominal pain, cough, back pain, fatigue, nausea, arthralgia, diarrhea and dyspepsia were reported in ≥ 5% of subjects in clinical studies.

Drug interactions: Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin. Antimycobacterial: rifabutin, rifampin, rifapentine. Herbal Products: St. John's wort. Drugs that reduce renal function or compete for active tubular secretion such as acyclovir, cidofovir, ganciclovir, valacyclovir, valganciclovir, aminoglycosides (e.g., gentamicin), and high-dose or multiple NSAIDs.

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