

WHATS NEW IN GASTROENTEROLOGY



**CHARLENE LEPANE DO MSPH FACG
FACOI
GASTROENTEROLOGIST
ORLANDO VAMC**

******NO DISCLOSURES******

COLORECTAL CANCER (April 16)



- 2016 FDA approved a second generation serum assay for detection of circulating methylated Septin 9 for CRC screening (1)
 - Detects Septin 9 DNA which is hypermethylated in CRC but not in normal tissue
 - Intended for average risk patients who refuse guideline recommended screening methods
 - Positive serum test should be followed up with a colonoscopy
 - Until further evidence is available, serum tests for CRC screening are not recommended

COLORECTAL CANCER



- First generation stool DNA test was withdrawn in 2012
- Newer test, Cologuard, combines stool DNA testing using a gene amplification technique (to allow detection of low frequency mutations with increased sensitivity for advanced adenomas), for patterns of DNA methylation and with testing for hemoglobin
- Cologuard vS fecal immunochemical test (FIT) demonstrated sensitivity of 92.3% vs 73.8% in one test (2) (*NEJM*)
- Sensitivity of the DNA test was not affected by cancer stage or location of the lesion
- Based on above data, Cologuard approved by FDA 2014 as a screening test for CRC (if positive followed by colonoscopy) (3)

COLORECTAL CANCER



- The implications of "false positives," abnormal DNA testing in patients who are not found to have colonic lesions on colonoscopy, is uncertain
- In a study of screening with three modalities (stool DNA, colonoscopy, and fecal immunochemical tests) in average-risk patients, nearly 10 percent of those with an entirely negative colonoscopy had a positive stool DNA test (4) (*NEJM*)
- The appropriate interval between screening fecal DNA tests is unknown
- Centers for Medicare and Medicaid Services (CMS) include coverage for this test once every three years for asymptomatic Medicare beneficiaries age 50 to 84 years at average risk for CRC as of 10/14 (5)

UPDATED GUIDELINES FOR ENDOSCOPIC SURVEILLANCE AFTER CRC TX (March 16)



- Flexible sigmoidoscopy or EUS every 3-6 months for the first 2-3 years after surgery for rectal cancer for those at risk for local recurrence (6)
(*Gastroenterology*)
 - Localized rectal cancer who have undergone surgery without total mesorectal excision (TME)
 - Those who have undergone transanal local excision or endoscopic submucosal dissection alone
 - Those with locally advanced rectal cancer who didn't receive neoadjuvant chemoradiotherapy followed by TME

HELICOBACTER PYLORI (June 16)



- The Toronto consensus has published new guidelines for the treatment of *Helicobacter pylori* in adults (7) (*Gastroenterology*)
 - These guidelines recommend a longer duration of treatment for all eradication regimens (14 versus 10 days)
 - limiting the use of triple therapy to areas with low clarithromycin resistance or high eradication rates
 - using quadruple (bismuth-containing or non-bismuth) therapy as a first line in all other areas
 - ✦ Bismuth-containing quadruple therapy consists of a PPI, combined with bismuth subsalicylate (524 mg four times daily) and two antibiotics (eg, metronidazole 250 mg four times daily and tetracycline 500 mg four times daily) given for 14 days
 - ✦ If tetracycline is not available, doxycycline (100 mg twice daily) may be substituted

H. PYLORI ERADICATION AND RISK OF GASTRIC CANCER (May 16)



- It has been unclear if eradication of *Helicobacter pylori* infection reduces the risk of gastric cancer among asymptomatic individuals in populations that are not at high risk for gastric cancer
- A meta-analysis of 27 studies included approximately 48,000 individuals, among whom 4800 were infected with *H. pylori* and approximately 700 had incident gastric cancers (8)
(*Gastroenterology*)
 - Individuals with eradication of *H. pylori* had a lower incidence of gastric cancer compared with those who did not receive eradication therapy

VONOPRAZAN-BASED TRIPLE THERAPY FOR H. PYLORI ERADICATION (March 16)



- Vonoprazan is a novel oral potassium-competitive acid blocker (PCAB)
- In a randomized trial, 650 H. pylori-positive patients with a history of a gastric or duodenal ulcer were assigned to first-line triple therapy with amoxicillin, clarithromycin, and either lansoprazole or vonoprazan (9) (*Gut*)
 - Patients failing first-line therapy received open-label second-line therapy with vonoprazan, amoxicillin, and metronidazole
 - Vonoprazan-based first-line therapy was non-inferior to lansoprazole-based therapy with H. pylori eradication rates of 93 and 76 percent, respectively.
 - There were no significant differences in adverse effects. The eradication rate with vonoprazan-based second-line triple therapy was 98 percent
 - Vonoprazan may be an effective option for H. pylori eradication in combination with antibiotics; however, further studies are needed

PROTON PUMP INHIBITORS AND RISK OF DEMENTIA IN OLDER ADULTS (Feb 16)



- A new study has identified a possible link between proton pump inhibitors (PPIs) and risk of dementia in older adults
- In a prospective cohort study of >73,000 adults aged 75 years and older who were free of dementia at baseline, regular use of a PPI was associated with a 1.4-fold increase in the risk of incident dementia, independent of age, gender, depression, stroke, heart disease, and polypharmacy (10) (*JAMA*)
 - Possible factors that could contribute to this finding include PPI-induced vitamin B12 deficiency or an interaction between PPIs and amyloid beta deposition, although these factors were not examined in this study
 - More studies are needed to confirm or refute this association

DEFIBROTIDE FOR HEPATIC SINUSOIDAL OBSTRUCTION SYNDROME (April 16)



- Hepatic sinusoidal obstruction syndrome (SOS) is an uncommon but serious complication of allogeneic hematopoietic cell transplantation (HCT)
- It accounts for a significant fraction of transplant-related mortality and, in its severe form, is almost always fatal when treated with supportive care alone
- Small single-arm prospective trials have demonstrated modest improvement in patients with severe SOS treated with defibrotide
- In the largest international study, 102 adults and children with SOS and multiorgan failure were treated with defibrotide (11) (*Blood*)
 - When compared with historical controls, defibrotide was associated with higher response rates and improved survival (38 versus 25 percent at day +100)
 - Based on this and other studies, defibrotide has been approved by the US Food and Drug Administration for the treatment of severe SOS (12)
 - It is our preferred therapy for such patients

LIVER CANCER DEATH RATES INCREASING IN THE US (March 16)



- Over the past 30 years, death rates in the United States have declined for all common cancers (eg, breast, prostate, and lung), with the exception of liver cancer
- In the Annual Report to the Nation on the Status of Cancer, 1975-2012, the overall cancer death rates for men and women of all major racial and ethnic populations decreased by 1.5 percent per year between 2003 and 2012 (13) (*Cancer*)
- However, during this same period, liver cancer death rates increased by 2.8 percent per year in men and 3.4 percent per year in women, while liver cancer incidence rates increased by 3.5 percent per year in men and 3 percent per year in women

CT-COLONOGRAPHY VS COLONOSCOPY FOR SSA POLYPS



- Sessile serrated adenomatous polyps (SSPs) are suggested to be the precursors of 15–30% of all colorectal cancers (CRCs)
- Randomized controlled trial compared CTC with colonoscopy for population screening were used for the analysis (*Am J Gastro*)
- The current CTC strategy showed a marked lower detection for especially flat high-risk SSPs (17 vs. 0), high-risk SSP located in the proximal colon (32 vs. 1), and SSPs with dysplasia (30 vs. 1)
- The detection rate of high-risk SSPs was significantly higher with colonoscopy than CTC (14)

ZIKA VIRUS AND TISSUE DONATION (March 16)



- Zika virus has been detected in a number of tissues and body fluids
- To avoid possible transmission of Zika virus infection, the US Food and Drug Administration (FDA) has issued donor deferral recommendations for hematopoietic stem cells, tissues, and donor sperm or eggs; the recommendations do not apply to solid organs (15)
- Living donors with Zika virus infection or relevant epidemiologic exposure (residence in or travel to an area where mosquito-borne transmission of Zika virus infection has been reported, or unprotected sexual contact with a person who meets these criteria) should be considered ineligible for donation for six months
- Deceased donors with Zika virus infection in the preceding six months should also be considered ineligible
- The deferral period recommended by the FDA for blood donors with risk factors for Zika virus infection remains at four weeks

HCV TREATMENT IN RENAL FAILURE PATIENTS (Feb 16)



- Despite the proliferation of interferon-free regimens for the treatment of chronic hepatitis C (HCV) infection, safety concerns have limited options for patients with severe renal impairment, who have been excluded from trials of most available regimens
- In January 2016, the US Food and Drug Administration approved the new combination regimen elbasvir-grazoprevir (Zepatier) for the treatment of patients with genotypes 1 and 4 HCV infection, including those with any degree of renal impairment (including dialysis dependence)
- In a randomized, placebo-controlled trial of genotype 1-infected patients with estimated glomerular filtration rate (eGFR) <30 mL/min per 1.73 m², the sustained virologic response (SVR) rate was 94 percent among the 122 patients who received elbasvir-grazoprevir for 12 weeks, and adverse event rates were similar between treatment and placebo groups (16) (*Lancet*)
- These results were comparable to those among patients with normal renal function

HBV REACTIVATION IN PATIENTS UNDERGOING CHEMOTHERAPY FOR SOLID TUMORS (Jan 16)



- Patients with serologic evidence of hepatitis B virus (HBV) infection (hepatitis B surface antigen [HBsAg]-positive or hepatitis B core antibody [anti-HBc]-positive) are at risk for HBV reactivation if they receive immunosuppressive therapy
- The magnitude of risk for patients receiving chemotherapy for solid tumors has not been well established
- In a systematic review of such patients, the risk of reactivation among those who were HBsAg-positive ranged from 4 to 68 percent, with most studies reporting a reactivation risk greater than 10 percent (17) (*Annals IM*)
- Antiviral therapy administered during chemotherapy was associated with an approximately 90 percent reduction in HBV reactivation risk as well as reductions in HBV-related hepatitis and the need for chemotherapy interruption
- Although some expert groups disagree, we check HBV serologies before initiating therapy with any potentially immunosuppressive chemotherapy
- Our recommendations for prophylactic antiviral therapy depend upon the HBsAg status of the patient and the type of chemotherapy used

EPCLUSA (June 16)



- Epclusa (Gilead) (Sofosbuvir + velpatasvir) NS5A Inhibitor + NS5B Polymerase Inhibitor
- Approved June 2016
- Treatment of genotype 1,2,3,4,5,6 chronic hepatitis C for non-cirrhosis, compensated cirrhosis and with ribavirin for decompensated cirrhosis

68-Ga DOTATATE FOR IMAGING OF NEUROENDOCRINE TUMORS (June 16)



- Most well-differentiated neuroendocrine tumors arising in the gastrointestinal tract, pancreas, bronchus, and other sites express somatostatin receptors, and they can be imaged using radiolabeled somatostatin analogs
- Uptake of radiolabeled somatostatin analogs is predictive of a clinical response to somatostatin analogs such as octreotide, and a positive scan can also identify an otherwise occult primary site in patients presenting with metastatic disease
- Newer positron-emitting somatostatin analogs such as 68-Ga DOTATATE have emerged which, when combined with high-resolution positron emission tomography (PET) scanning, are more sensitive than conventional 111-In pentetreotide imaging (OctreoScan) for detection of small lesions (18) (*J Clin Onc*)
- A kit for preparation of 68-Ga DOTATATE injection as a radioactive diagnostic agent for PET imaging (Netspot) was approved by the US Food and Drug Administration in June 2016 (19)
- Due to its greater sensitivity, 68-Ga DOTATATE PET may be preferred over conventional 111-In pentetreotide scanning where available

ADVERSE OUTCOMES WITHOUT F/U OF BILIARY COLIC FROM ER (April 16)



- Proper follow-up of patients being discharged from the emergency department following an episode of symptomatic gallstones is important to avoid adverse outcomes
- This was examined in a study of more than 11,000 Texas Medicare patients age 66 and older with symptomatic gallstones who were discharged from the emergency department without undergoing cholecystectomy (20) (*J Am Coll Surg*)
- A quarter of the patients did not see a physician in follow-up
- Subsequent emergency hospitalization was required in 78 percent of those patients (compared with 8 percent of those who saw a surgeon and 15 percent of those who saw a physician other than a surgeon)
- Of the patients with biliary colic, 17 percent required emergency cholecystectomy, with a complication rate of 41 percent (compared with a 19 percent complication rate for elective cholecystectomy)
- This study reinforces the importance of appropriate follow-up and management for patients with symptomatic gallstones

UNDERUTILIZATION OF ENZYMES IN PANCREATIC CANCER (April 16)

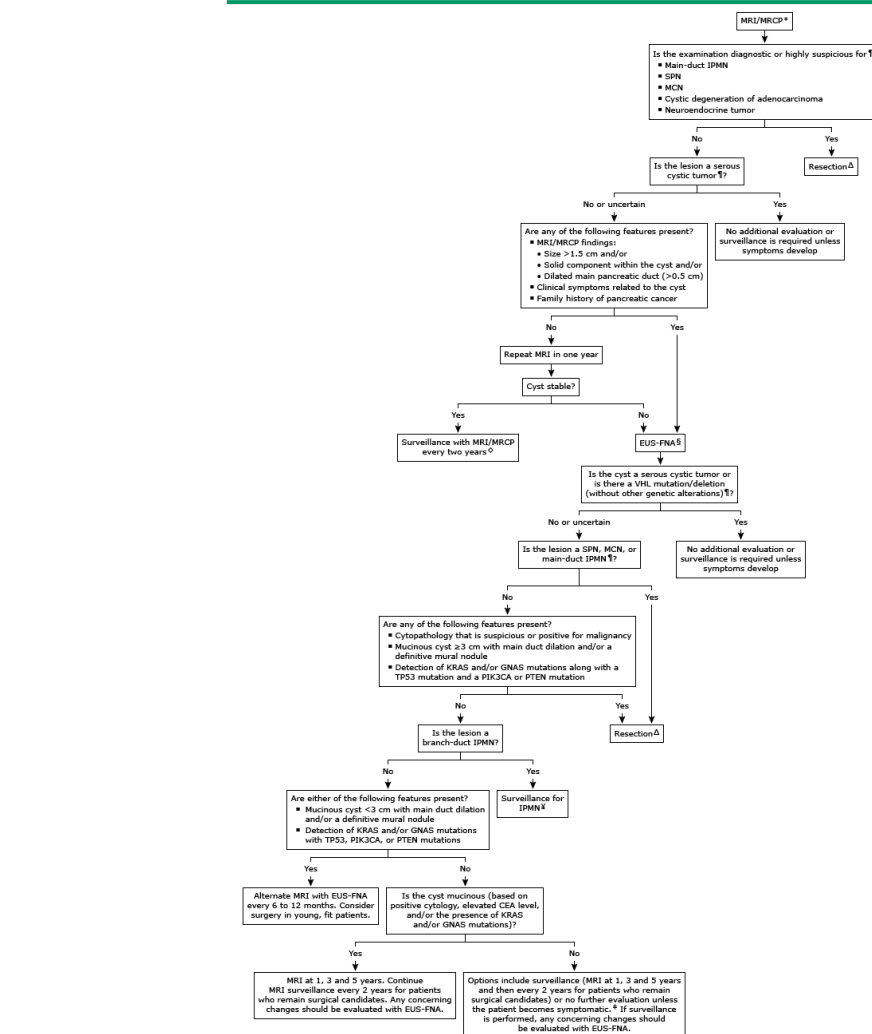


- Patients with advanced pancreatic cancer often have pancreatic exocrine insufficiency leading to maldigestion, fat malabsorption, steatorrhea, and weight loss
- These patients should be treated empirically with oral pancreatic enzyme replacement therapy (PERT), evidence suggests that PERT is underutilized (21) *BMJ Support Palliat Care*
- In a review of 129 patients with metastatic pancreatic cancer, over 70 percent had symptoms that could be attributed to malabsorption, yet only 21 percent were prescribed PERT

AGA GUIDELINES AND EVALUATION OF PANCREATIC CYSTS (Feb 16)



- The optimal approach to evaluating pancreatic cysts is unclear
- AGA published guidelines on the evaluation and management of pancreatic cysts 2015(22) *Gastroenterology*
- Data suggests if the AGA guidelines are applied, many cysts with advanced neoplasia will be missed (23) *Gastrointestinal Endoscopy*
- In a series of patients who underwent EUS with FNA of pancreatic cysts, the AGA guideline was 62 percent sensitive and 79 percent specific for detecting advanced neoplasia, and missed 45 percent of IPMN with adenocarcinoma or high-grade dysplasia
- UpToDate authors advise a lower threshold for evaluating cysts (algorithm 5) than in the AGA guideline



Published guidelines on the management of pancreatic cystic neoplasms are variable. This algorithm reflects the authors' approach. Refer to UpToDate topic reviews on pancreatic cystic neoplasms for additional details.

MRI: magnetic resonance imaging; MRCP: magnetic resonance cholangiopancreatography; IPMN: intraductal pancreatic mucinous neoplasm; SPN: solid pseudopapillary neoplasm; MCN: mucinous cystic neoplasm; EUS-FNA: endoscopic ultrasound-guided fine-needle aspiration; CEA: carcinoembryonic antigen.

* A pancreatic protocol computed tomography scan is an alternative for patients who cannot undergo MRI.

† Refer to UpToDate topics on the evaluation of pancreatic cystic neoplasms for details on the specific features needed to make a diagnosis.

Δ The decision to recommend surgery should take into account factors such as the patient's age and general health, the malignant risk of the specific lesion, and the suspicion for malignancy.

◊ Surveillance should be considered because these cysts, despite being small, may be precancerous. The decision to pursue surveillance should take into account factors such as the patient's age, comorbidities, and willingness to undergo surgery if worrisome features develop.

§ Cyst fluid should be tested for cytology; CEA level; and the molecular markers KRAS, GNAS, VHL, CTNNB1, TP53, PIK3CA, and PTEN. KRAS and GNAS have been associated with IPMNs and MCNs, and GNAS appears to be highly specific for IPMN. TP53, PIK3CA, and PTEN have been associated with high-grade dysplasia or invasive carcinoma in patients with IPMN. VHL is seen in serous cystic tumors, whereas CTNNB1 is seen in SPNs.

‡ Refer to UpToDate topic on the management of IPMNs for details.

‡ Refer to UpToDate content on the management of pancreatic cysts for details.

ORAL VACCINE TO PREVENT CHOLERA IN HIGH-RISK TRAVELERS (June 16)



- Cholera, caused by infection with the bacterium *Vibrio cholerae*, is characterized by severe watery diarrhea, which can rapidly lead to dehydration
- In June 2016, a live attenuated oral cholera vaccine (Vaxchora) was approved by the US FDA for prevention of cholera caused by serogroup O1 in adults 18 through 64 years
- Those who warrant vaccination include aid, refugee, and health care workers planning to work among or near displaced populations in endemic or epidemic settings, and long-stay travelers in very high-risk countries
- a single dose of vaccine given prior to an oral challenge with a *V. cholerae* O1 strain was 90% effective (@10 Days) and 80% (@3 mo) in preventing moderate to severe cholera (24) *Clin Infect Dis*

ROME IV CRITERIA FOR FUNCTIONAL GI DISORDERS (June 16)



- The Rome Foundation has released revised criteria (Rome IV) for the diagnosis of functional gastrointestinal disorders (25) *Gasroenterology*
- Revisions include:
 - changes to the criteria for IBS and its subtypes (used with Bristol Stool Form Scale)
 - new criteria for reflux hypersensitivity
 - inclusion of diagnoses with known etiologies that alter gut-brain interaction (eg, opioid-induced constipation)

DIAGNOSTIC CRITERIA FOR OPIOID INDUCED CONSTIPATION (May 16)



- The diagnosis of opioid induced constipation (OIC) should be based upon clinical history, physical examination (including a rectal examination) and limited diagnostic tests
- Diagnostic criteria for OIC per ROME-IV criteria include new or worsening symptoms of constipation when initiating, changing, or increasing opioid therapy that must include two or more of the following:
 - Straining during more than one-fourth of defecations
 - Lumpy or hard stools more than one-fourth of defecations
 - Sensation of incomplete evacuation more than one-fourth of defecations
 - Sensation of anorectal obstruction/blockage more than one-fourth of defecations
 - Manual maneuvers to facilitate more than one-fourth of defecations (eg, digital evacuation, support of the pelvic floor)
 - Fewer than three spontaneous bowel movements per week

OZANIMOD FOR ULCERATIVE COLITIS (May 16)



- Ozanimod, an experimental agent, is an oral agonist of the sphingosine-1-phosphate receptor subtypes 1 and 5 that decreases circulating activated lymphocytes
- In a randomized trial, 197 patients with moderate to severe ulcerative colitis were assigned to ozanimod (1 mg or 0.5 mg daily) or placebo for 32 weeks (26) *NEJM*
- At eight weeks, patients treated with the higher dose of ozanimod had a slightly higher rate of clinical remission compared with placebo (16 versus 6 percent)
- There were no significant differences in adverse effects between the groups
- Larger trials with extended treatment are needed to establish the clinical efficacy and safety of ozanimod

SKIN DISORDERS ASSOCIATED WITH TNF INHIBITOR USE (Feb 16)



- A variety of skin disorders have been reported in association with the use of TNF's
- Cohort of 917 patients with IBD on TNF inhibitors for a median of 3.5 years where 29 percent developed skin lesions (12.4 per 100 patient-years) (27) *Ann Intern Med*
- Cutaneous lesions included (most to least common) psoriasiform eczema, eczema, xerosis cutis, palmoplantar pustulosis, and psoriasis; other abnormalities were mostly infectious and inflammatory skin lesions and alopecia
- The majority of patients were managed without discontinuation of TNF inhibitor therapy

OUTBREAK OF BURKHOLDERIA CEPACIA INFECTION ASSOCIATED WITH CONTAMINATED ORAL LIQUID DOCUSATE

- In June 2016, a multistate outbreak of Burkholderia cepacia infection was reported in the US by the CDC
- B. cepacia typically causes lung colonization and infection in patients with cystic fibrosis (CF), but most cases in this outbreak have involved mechanically ventilated intensive care unit patients without CF
- Because cases in one state have been associated with contaminated oral liquid docusate, the CDC recommends that facilities not use liquid docusate products for any patient
- PharmaTech LLC, the manufacturer of the contaminated product, Diocto Liquid, has voluntarily recalled all non-expired lots

REFERENCES



1. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/MolecularandClinicalGeneticsPanel/UCM390238.pdf>
2. Multitarget stool DNA testing for colorectal-cancer screening. Imperiale TF, Ransohoff DF, Itzkowitz SH, Levin TR, Lavin P, Lidgard GP, Ahlquist DA, Berger BM *N Engl J Med*. 2014;370(14):1287
3. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm409021.htm>
4. Multitarget stool DNA testing for colorectal-cancer screening. Imperiale TF, Ransohoff DF, Itzkowitz SH, Levin TR, Lavin P, Lidgard GP, Ahlquist DA, Berger BM *N Engl J Med*. 2014;370(14):1287
5. <http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=277>
6. Colonoscopy Surveillance After Colorectal Cancer Resection: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. Kahi CJ, Boland CR, Dominitz JA, Giardiello FM, Johnson DA, Kaltenbach T, Lieberman D, Levin TR, Robertson DJ, Rex DK *Gastroenterology*. 2016 Mar;150(3):758-768.e11. Epub 2016 Feb 10
7. The Toronto Consensus for the Treatment of Helicobacter pylori Infection in Adults. Fallone CA, Chiba N, van Zanten SV, Fischbach L, Gisbert JP, Hunt RH, Jones NL, Render C, Leontiadis GI, Moayyedi P, Marshall JK *Gastroenterology*. 2016;151(1):51.

REFERENCES



8. Association Between *Helicobacter pylori* Eradication and Gastric Cancer Incidence: A Systematic Review and Meta-analysis. Lee YC, Chiang TH, Chou CK, Tu YK, Liao WC, Wu MS, Graham DY *Gastroenterology*. 2016 May;150(5):1113-1124.e5. Epub 2016 Feb 2
9. Vonoprazan, a novel potassium-competitive acid blocker, as a component of first-line and second-line triple therapy for *Helicobacter pylori* eradication: a phase III, randomised, double-blind study. Murakami K, Sakurai Y, Shiino M, Funao N, Nishimura A, Asaka M *Gut*. 2016 Mar
10. Association of Proton Pump Inhibitors With Risk of Dementia: A Pharmacoepidemiological Claims Data Analysis. Gomm W, von Holt K, Thomé F, Broich K, Maier W, Fink A, Doblhammer G, Haenisch B *JAMA Neurol*. 2016;73(4):410
11. Phase 3 trial of defibrotide for the treatment of severe veno-occlusive disease and multi-organ failure. Richardson PG, Riches ML, Kernan NA, Brochstein JA, Mineishi S, Termuhlen AM, Arai S, Grupp SA, Guinan EC, Martin PL, Steinbach G, Krishnan A, Nemecek ER, Giralt S, Rodriguez T, Duerst R, Doyle J, Antin JH, Smith A, Lehmann L, Champlin R, Gillio A, Bajwa R, D'Agostino RB Sr, Massaro J, Warren D, Miloslavsky M, Hume RL, Iacobelli M, Nejadnik B, Hannah AL, Soiffer RJ *Blood*. 2016;127(13):1656
12. http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208114lbl.pdf
13. Annual Report to the Nation on the Status of Cancer, 1975-2012, featuring the increasing incidence of liver cancer. Ryerson AB, Ehemann CR, Altekruse SF, Ward JW, Jemal A, Sherman RL, Henley SJ, Holtzman D, Lake A, Noone AM, Anderson RN, Ma J, Ly KN, Cronin KA, Penberthy L, Kohler BA *Cancer*. 2016;122(9):1312

REFERENCES



14. CT-Colonography vs. Colonoscopy for Detection of High-Risk Sessile Serrated Polyps J.E.G. IJspeert, MD; C.J. Tutein Nolthenius, MD; E.J. Kuipers, MD, PhD; M.E. van Leerdam, MD, PhD; C.Y. Nio, MD, PhD; M.G.J. Thomeer, MD, PhD; K. Biermann, MD, PhD; M.J. van de Vijver, MD, PhD; E. Dekker, MD, PhD; J. Stoker, MD, PhD *Am J Gastroenterol.* 2016;111(4):516-522.
15. <http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM488582.pdf>
16. Grazoprevir plus elbasvir in treatment-naïve and treatment-experienced patients with hepatitis C virus genotype 1 infection and stage 4-5 chronic kidney disease (the C-SURFER study): a combination phase 3 study. Roth D, Nelson DR, Bruchfeld A, Liapakis A, Silva M, Monsour H Jr, Martin P, Pol S, Londoño MC, Hassanein T, Zamor PJ, Zuckerman E, Wan S, Jackson B, Nguyen BY, Robertson M, Barr E, Wahl J, Greaves W *Lancet.* 2015;386(10003):1537
17. Hepatitis B Virus Reactivation and Prophylaxis During Solid Tumor Chemotherapy: A Systematic Review and Meta-analysis. Paul S, Saxena A, Terrin N, Viveiros K, Balk EM, Wong JB *Ann Intern Med.* 2016 Jan;164(1):30-40. Epub 2015 Nov 24
18. Prospective Study of 68Ga-DOTATATE Positron Emission Tomography/Computed Tomography for Detecting Gastro-Entero-Pancreatic Neuroendocrine Tumors and Unknown Primary Sites. Sadowski SM, Neychev V, Millo C, Shih J, Nilubol N, Herscovitch P, Pacak K, Marx SJ, Kebebew E *J Clin Oncol.* 2016 Feb;34(6):588-96. Epub 2015 Dec 28
19. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm504524.htm>

REFERENCES



20. Trends in Follow-Up of Patients Presenting to the Emergency Department with Symptomatic Cholelithiasis. Dimou FM, Adhikari D, Mehta HB, Riall TS *J Am Coll Surg*. 2016 Apr;222(4):377-84. Epub 2015 Dec 21
21. Pancreatic enzyme replacement therapy (PERT) for malabsorption in patients with metastatic pancreatic cancer. Landers A, Muircroft W, Brown H
BMJ Support Palliat Care. 2016 Mar;6(1):75-9. Epub 2014 Aug 27
22. American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Vege SS, Ziring B, Jain R, Moayyedi P, Clinical Guidelines Committee. *Gastroenterology*. 2015 Apr;148(4):819-22
23. American Gastroenterological Association guidelines are inaccurate in detecting pancreatic cysts with advanced neoplasia: a clinicopathologic study of 225 patients with supporting molecular data. Singhi AD, Zeh HJ, Brand RE, Nikiforova MN, Chennat JS, Fasanella KE, Khalid A, Papachristou GI, Slivka A, Hogg M, Lee KK, Tsung A, Zureikat AH, McGrath K *Gastrointest Endosc*. 2016;83(6):1107
24. Single-dose Live Oral Cholera Vaccine CVD 103-HgR Protects Against Human Experimental Infection With *Vibrio cholerae* O1 El Tor. Chen WH, Cohen MB, Kirkpatrick BD, Brady RC, Galloway D, Gurwith M, Hall RH, Kessler RA, Lock M, Haney D, Lyon CE, Pasetti MF, Simon JK, Szabo F, Tennant S, Levine MM *Clin Infect Dis*. 2016 Jun;62(11):1329-35. Epub 2016 Mar 21
25. Bowel Disorders. Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R *Gastroenterology*. 2016 Feb

REFERENCES



26. Ozanimod Induction and Maintenance Treatment for Ulcerative Colitis. Sandborn WJ, Feagan BG, Wolf DC, D'Haens G, Vermeire S, Hanauer SB, Ghosh S, Smith H, Cravets M, Frohna PA, Aranda R, Gujrathi S, Olson A, TOUCHSTONE Study Group N Engl J Med. 2016 May;374(18):1754-1762
27. Characteristics of Skin Lesions Associated With Anti-Tumor Necrosis Factor Therapy in Patients With Inflammatory Bowel Disease: A Cohort Study. Cleynen I, Van Moerkercke W, Billiet T, Vandecandelaere P, Vande Casteele N, Breynaert C, Ballet V, Ferrante M, Noman M, Assche GV, Rutgeerts P, van den Oord JJ, Gils A, Segaert S, Vermeire S Ann Intern Med. 2016;164(1):10
27. US Food and Drug Administration. Oral liquid docusate sodium by PharmaTech: Recall - contaminated with B. cepacia.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm511528.htm> (Accessed on July 19, 2016)



THANK YOU