H. Pylori-Associated Gastric Mucosal Lymphoma and Risk For Secondary Cancers

Cure of Helicobacter pylori infection induces remission in most patients with gastric mucosa-associated lymphoid tissue lymphoma (GML). To determine the long-term outcomes of these patients in a prospective, multi-center trial and investigate development of second cancers or potential histologic residual disease, 120 patients were followed with Stage E-11 GML for a median of 122 months after H. pylori eradication. Remission was determined by histology analysis and development of second cancers was documented.

Of the patients, 80% achieved complete remission from GML, and 80% of those remained disease-free. Estimated mean survival time in the Kaplan-Meier Analysis was 147 months (138 to 156 months). Of the patients that achieved complete remission, 17% (16 of 96) had histologic residual disease after a median of 32 months. Disease did not progress in any of these patients and all but one achieved a second complete remission.

Standardized morbidity rates revealed a significantly higher incidence of gastric cancer (8.567), or non-Hodgkin's lymphoma (18.621), in the 96 patients that achieved a complete remission compared with the general German population.

It was concluded that cure of H. pylori infection leads to continuous complete remission in most patients with H. pylori-associated GML. Patients are at risk for development of secondary cancers (i.e., gastric cancer and non-Hodgkin's lymphoma).

Ed. Note: Appropriate surveillance is indicated.

Wundisch, T., Dieckhoff, P., Greene, B., et al. "Second Cancers and Residual Disease in Patients Treated For Gastric Mucosa-Associated Lymphoid Tissue Lymphoma By Helicobacter Pylori Eradication and Followed for Ten Years." Gastroenterology, 2012; Vol. 143, pp. 936-942.

Gastric and Esophageal Malignancies are Increased in People with AIDS

To evaluate the risks of different histologic and anatomic subtypes of carcinomas and non-Hodgkin's lymphomas (NHLs) of the stomach and esophagus in people with AIDS, data was analyzed from the HIV-AIDS Cancer Match Study, which linked data collected from 1980 to 2007 for 16 US population-based HIV and AIDS and cancer registries.

Risks of stomach and esophageal malignancies in people with AIDS (596,955), with those of the general population using standardized incidence ratios (SIRs) were evaluated. Calendar trends were assessed using Poisson regression.

People with AIDS had increased risk of carcinoma of the esophagus (SIR 1.69) and stomach (SIR 1.44). Risk was increased for esophageal carcinoma (SIR 1.91), and squamous cell carcinoma (SIR 1.47). People with AIDS had greater risk of carcinoma of the gastric cardia (SIR 1.36) and noncardia (SIR 1.53). Compared with the general population, most stomach and esophageal NHLs developed in people with AIDS were diffuse large B-cell lymphomas, but these individuals also had an increased risk of gastric mucosa-associated lymphoid tissue lymphoma (SIR 5.99).

The incidence of carcinomas remained fairly constant over time, but rates of NHL decreased from 1980 to 2007.

It was concluded that people with AIDS are at increased risk for developing esophageal and stomach carcinomas and NHLs, although the incidence of NHL decreased from 1980 to 2007 as treatments for HIV infection improved. HIV-infected individuals face continued risks of esophageal and stomach carcinomas.

Persson, E., Shiels, M., Dawsey, S., et al. "Increased Risk of Stomach and Esophageal Malignancies in People with AIDS." Gastroenterology, 2012; Vol. 143, pp. 943-950.

EUS-FNA in Diagnosis of Autoimmune Pancreatitis

To determine whether EUS-guided FNA by using 22-gauge needles is useful for the diagnosis or evaluation of autoimmune pancreatitis (AIP), a retrospective study was carried out in which a total of 273 patients, including 25 with AIP, underwent EUS-FNA and histologic examination. This procedure using 22-G needles provided adequate tissue samples for histopathologic evaluation because more than 10 high-power fields were available for evaluation in 20 of 25 patients (80%).

The mean immunoglobulin-G4 positive cell count was 13.7/high-power field. Obliterative phlebitis was observed in 10 of 25 patients (40%), in the context of the ICD criteria for AIP, with 14 and 6 of 25 patients judged to have Level 1 (positive for three or four

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items), and Level 2 (positive for two items), histologic findings, respectively, meaning that 20 of 25 patients were suggested to have lymphoplasmacytic sclerosing pancreatitis based on the ICD criteria. The diagnosis in one patient was Type 2 AIP because a granulocytic epithelial lesion was identified in this patient.

In this retrospective study with a small number of patients, the results suggest that EUS-FNA by using 22-gauge needles provides tissue samples adequate for histopathologic evaluation and greatly contributes to the histologic diagnosis of AIP.

Kanno, A., Ishida, K., Hamada, S., et al. "Diagnosis of Autoimmune Pancreatitis by EUS-FNA by Using a 22-Gauge Needle Based on the International Consensus Diagnostic Criteria." Gastrointestinal Endoscopy, 2012; Vol. 76, pp. 594-602.

Effect of Inadequate Bowel Preparation on Screening Colonoscopy

To determine the prevalence of missed adenomas on average-risk patients presenting for screening colonoscopy who are found to have inadequate bowel preparation, a retrospective chart review was carried out with endoscopic and pathology reports examined to determine the characteristics of polyps. Data from repeat colonoscopies were collected through 2010 at an outpatient endoscopic center as part of an academic medical center.

The study involved patients who underwent outpatient average-risk screening colonoscopy between 2004 and 2009 that were documented to have the inadequate bowel preparation and with colonoscopy to the cecum.

Initial adenoma detection rate and adenoma detection rate on followup examination was measured. Inadequate bowel preparation was reported on 373 patients with an initial adenoma detection rate of 25.7% of 133 patients who underwent repeat colonoscopy. A total of 33.8% had at least one adenoma detected and 18% had high-risk states detected, including greater than 3 adenomas, an adenoma greater than 1 cm, or adenoma with villous features or high-grade dysplasia.

Per adenoma miss rate was 47.9% among patients with at least one adenoma on repeat colonoscopy, 31.1% had no polyps on initial colonoscopy. The mean time between colonoscopies was 340 days.

Among patients with high-risk states, 25% had no polyps on initial colonoscopy and the mean time between colonoscopies was 271 days. The study was limited by its retrospective design.

It was concluded that adenomas and high-risk lesions were frequently detected on repeat colonoscopy in patients with inadequate bowel preparation on initial screening colonoscopy, suggesting that these lesions were likely missed on initial colonoscopy.

Chokshi, R., Hovis, C., Hollander, T., et al. "Prevalence of Missed Adenomas in Patients With Inadequate Bowel Preparation on Screening Colonoscopy." Gastrointestinal Endoscopy 2012; Vol. 75, pp. 1197-2003.

Cocaine-Related Ischemic Colitis

A retrospective review of medical records at two affiliated teaching hospitals located in a downtown area of Milwaukee was carried out over a 9-year period. A total of 208 patients were identified by ICD-9 codes with a confirmed diagnosis of bowel ischemia, with imaging and endoscopic findings and self-report of recent cocaine use or positive urine toxicology screen within 6 months of a hospital admission for ischemia. Controls were individuals who met the same criteria without cocaine use and a negative urine test for cocaine.

Patients with cocaine-related ischemia were significantly younger and had a significantly higher mortality rate than patients with ischemic colitis unrelated to cocaine. The cause of death in all cases was septic shock caused by extensive bowel ischemia. Multivariate logistic regression analysis showed that cocaine-related ischemic colitis was a significant risk factor for mortality, with an odds ratio of 5.77, and with need for surgical intervention.

It was concluded that cocaine-related ischemic colitis has a high mortality. In young patients presenting with acute abdominal pain and/or rectal bleeding with evidence of bowel wall thickening or pneumatosis on imaging studies or colonoscopy, cocaine-related ischemia should be considered and particularly to identify patients at high risk of sepsis and death.

El-Ramah, M., Einstein, M., Mori, N., Vakil, N. "High Mortality of Cocaine-Related Ischemic Colitis: A Hybrid Cohort/Case-Controlled Study." Gastrointestinal Endoscopy, 2012; Vol. 75, pp. 1226-1232.

Varying Appearance of Proximal Colorectal Neoplasms

To investigate the differences in endoscopic appearance (i.e., diminutive size and nonpolypoid shape), of proximal compared with distal colorectal neoplasms, endoscopists in the Netherlands who were previously trained in the detection and classification of nonpolypoid colorectal lesions, carried out examination on consecutive patients undergoing elective colonoscopy and including 3,720 patients.

The endoscopic appearance (i.e., diminutive size – less than 6 mm, or nonpolypoid shape – height less than one-half the diameter), of colorectal adenomas and serrated polyps (SPs), with a focus on adenomas with advanced histology included high-grade dysplasia or early CRC and SPs with dysplasia or large size.

In the 3,720 consecutive patients, there were 2,106 adenomas and 941 SPs. We found that in both men and women, proximal adenomas with high-grade dysplasia/early CRC (N = 181), were more likely to be diminutive or nonpolypoid than distal ones (76.3% vs. 26.2%). Of the proximal adenomas, 84.4% were diminutive or nonpolypoid, compared with 68% of the distal ones. Likewise, large and dysplastic SPs in the proximal colon were more often nonpolypoid than distal ones (66.2% vs. 27.8%).

It was concluded that proximal colorectal neoplasms with advanced histology frequently are small, or have a nonpolypoid appearance. These findings were considered to support careful inspection of the proximal colon, if quality of cancer prevention with the use of colonoscopy is to be optimized.

Rondagh, E., Bouwens, M., Riedo, R., et al. "Endoscopic Appearance of Proximal Colorectal Neoplasms and Potential Implications For Colonoscopy in Cancer Prevention." Gastrointestinal Endoscopy, 2012; Vol. 75, pp. 1218-1225.

Value of Split-Dose Preparation for Colonoscopy

To compare polyp detection rates (PDRs) and adenoma detection rates (ADRs) before and after the implementation of a split-dose preparation (SDP), as the preferred bowel preparation, this study was carried out. The secondary objectives were to compare the quality of the preparation and colonoscopy completion rates before and after implementation of the SDP. This was evaluated retrospectively in a tertiary medical care center with patients undergoing colonoscopy for screening and surveillance of colon polyps and cancer, with system-wide implementation of SDP.

A total of 3560 patients in the pre-SDP group and 1615 patients in the post-SDP group were included in the study. SDP use increased significantly from 9% to 74% after implementation. In comparison with the pre-SDP group, both PDRs (44.1% to 49.5%) and ADRs (26.7% to 31.8%), significantly improved in the post SDP group. The colonoscopy completion rate significantly increased from 93.6% to 95.5% in the post-SDP group. Bowel preparation quality also improved significantly in the post-SDP group.

It was concluded that system-wide implementation of an SDP as the primary choice for colonoscopy significantly improved both PDRs and ADRs, overall quality of the preparation, and colonoscopy completion rates.

Gurudu, S., Ramirez, F., Harrison, E., Leighton, J., Crowell, M. "Increased Adenoma Detection Rate with System-Wide Implementation of a Split-Dose Preparation for Colonoscopy." Gastrointestinal Endoscopy, 2012; Vol. 76, pp. 603-608.

Serrated Polyposis and Risk in Relatives For Carcinoma

In order to explore cancer risk for relatives of patients who have identified serrated polyps, including hyperplastic polyposis with serrated architecture in the colon and rectum, while the patients themselves are at increased risk of colorectal carcinoma, the aim of this study was to estimate the risks of CRC and extracolonic cancers for relatives of these patients.

A cohort of 1639 first and second-degree relatives of 100 indexed patients with serrated polyposis were included, regardless of the family history of polyps or cancer from genetic clinics in Australia, New Zealand, Canada, and the USA. These were retrospectively analyzed to estimate the country, age, and sex-specific standardized incidence ratios (SIRs) for relatives, compared with the general population.

A total of 102 CRCs were observed in first and second-relatives (SIR 2.25), with 54 in first-degree relatives (SIR 5.16), and 48 in second-degree relatives (SIR 1.38). Six pancreatic cancers were observed in first degree relatives (SIR 3.64). There was no statistical evidence of increased risk for cancer of the stomach, brain, breast, or prostate.

It was concluded that relatives of serrated polyposis patients are at significant increased risk of colorectal and pancreatic cancer and supporting the interpretation of a hereditary component.

Wyn, A., Walters, R., Buchanan, D., et al. "Cancer Risks For Relatives of Patients With Serrated Polyposis." American Journal of Gastroenterology 2012; Vol. 107, pp. 770-778.

Risk of HCC in Hepatitis B Patients with a Low HBV Load

To evaluate whether higher levels of HBsAg increase risk for hepatocellular carcinoma (HCC), a total of 2688 Taiwanese HBsAg-positive patients without evidence of cirrhosis were followed for a mean time period of 14.7 years. In addition to the known risk factors of HCC, the association between levels of HBsAg and the development of HCC were investigated.

Of the patients followed, 191 developed HCC with an average annual incidence rate of 0.5%. Baseline levels of HBsAg and HBV were associated with development of HCC and risk increase with increase in levels.

Compared to the HBsAg level, HBV DNA better predicted the development of HCC during 10 year and 15 year periods. However, evaluating hepatitis Be antigen-negative patients with levels of HBV DNA less than 2000 IU/mL, factors that determined HCC risk included sex, age, ALT and HBsAg 1000 international units or less, but did not follow the level of HBV DNA.

Multivariate analysis showed that the adjusted hazard ratio for HCC in patients with levels of HBsAg equal or greater than 1000 IU/mL versus less than 1000 IU/mL was 13.7.

It was concluded among patients infected with HBV genotype B or C that determinants of HCC risk include their sex, age, hepatitis Be antigen status, HBV genotype, and levels of alanine aminotransferase (ALT) and HBV DNA, but not the level of HBsAg. Among hepatitis Be antigen-negative patients with low viral loads, HCC risk is determined by levels of HBsAg and ALT and age, but not HBV DNA.

Tseng, T., Liu, C., Yang, H., et al. "High Levels of Hepatitis B Surface Antigen Increase Risk of Hepatocellular Carcinoma in Patients With Low HBV Load." Gastroenterology 2012; Vol. 142, pp. 1140-1149.

Crohn's Ileocolitis and Mucosal Healing with Adalimumab

To investigate the efficacy of adalimumab for inducing and maintaining mucosal healing in patients with Crohn's disease (CD), a randomized, double-blind, placebo-controlled trial (EXTEND) evaluated that drug for induction and maintenance of mucosal healing in 135 adults with moderate to severe ileocolonic CD. The baseline degree of mucosal ulceration was documented by ileocolonoscopy. All patients received induction therapy (subcutaneous adalimumab 160/80 mg at weeks 0/2, and at week 4 were randomly assigned to groups given 40 mg of medication or placebo every other week through week 52).

Open label adalimumab was given to patients with flares or no response starting at week 8. Mucosal healing was reassessed by ileocolonoscopy at weeks 12 and 52.

A total of 27% of patients receiving the drug had mucosal healing at week 12 versus 13% given placebo. At week 52, rates of mucosal healing were 24% and 0%, respectively. Remission rates based on Crohn's disease endoscopic index of severity were 52% for adalimumab and 28% for placebo at week 12, and 28% and 3%, respectively, at week 52.

Rates of clinical remission based on Crohn's disease activity index were greater among patients given continuous adalimumab therapy versus placebo at week 12 (47% versus 28%), and week 52 (33% versus 9%).

Five serious infections occurred during induction and four during open-label therapy. Three opportunistic infections, one in each group during double-blind therapy occurred, with one during open-label therapy reported.

It was concluded that following induction therapy with adalimumab, patients with moderately to severe active CD who continued to receive the drug are more likely to achieve mucosal healing than those given placebo.

Rutgeerts, P., Assche, G., Sandborn, W., et al. "Adalinumab Induces and Maintains Mucosal Healing in Patients With Crohn's Disease: Data From the EXTEND Trial." Gastroenterology 2012; Vol. 142, pp. 1102-1111

Murray H. Cohen, D.O., "From the Literature" Editor, is on the Editorial Board of *Practical Gastroenterology.*

SYNERGY PHARMACEUTICALS HIGHLIGHTS MECHANISTIC FEATURES OF PLECANATIDE, A NOVEL INVESTIGATIONAL DRUG FOR CHRONIC IDIOPATHIC CONSTIPATION

Scientific Poster Presentations at ACG 2012 and UEG Week

NEW YORK-- Synergy Pharmaceuticals Inc. (Nasdaq: SGYP), a developer of new drugs to treat gastrointestinal disorders and diseases, announced the preclinical findings being presented by Synergy scientists at two key gastroenterology congresses.

The scientific poster presentations describe the site of action and other mechanistic features of plecanatide, Synergy's investigational drug for the treatment of chronic idiopathic constipation (CIC) and constipation- predominant irritable bowel syndrome (IBS-C). Plecanatide is an agonist of the guanylate cyclase-C receptor and an analog of the natriuretic peptide, uroguanylin, the physiologic ligand of GC-C. As a uroguanylin analog, plecanatide is a member of a new class of non-systemic oral drugs, known as guanylate cyclase-C (GC-C) agonists, that act locally to promote intestinal fluid secretion.

"These preclinical studies helped to define plecanatide as the superior candidate for clinical testing in patients with chronic constipation," said Dr. Kunwar Shailubhai, Chief Scientific Officer of Synergy Pharmaceuticals, presented the data at the America College of Gastroenterology annual meeting in Las Vegas, NV. "In phase I and early phase II clinical testing, plecanatide exhibited an excellent safety profile, and patients in the phase IIa trial experienced relief from constipation without any remarkable diarrhea," said Stephen Comiskey, Synergy's Vice President for Product Development, who presented the preclinical data at the 20th United European Gastroenterology Week in Amsterdam, The Netherlands. "This summer Synergy achieved target enrollment in an ongoing phase IIb/III clinical trial of plecanatide in patients with chronic constipation, and we look forward to the results later this year."

Key preclinical findings being presented that informed the clinical testing of plecanatide as an optimal drug candidate include:

- Orally administered plecanatide acts primarily in the proximal intestine to stimulate water secretion essential for normalizing bowel movement.
- In vitro binding studies demonstrate that plecanatide binds to the same receptors in the proximal intestine as human uroguanylin.
- Plecanatide is highly stable and potent, with even greater affinity for the human GC-C receptors than the natural uroguanylin hormone.

"There is a compelling need to find safe and effective treatments for patients with CIC," said Douglas Drossman, Adjunct Professor of Medicine and Psychiatry and Co-Director Emeritus, UNC Center for Functional GI and Motility Disorders, UNC School of Medicine. "I am encouraged by the preclinical and early phase clinical data that demonstrate proof of concept for plecanatide as a treatment approach for chronic constipation, and look forward to seeing data from the ongoing trials."

Earlier this fall, in a poster session at the Joint International Neurogastroenterology and Motility Meeting, September 6-8, in Bologna, Italy, Synergy scientists also shared data describing the identification and selection of plecanatide (formerly SP-304) as the superior analog of uroguanylin based on physiochemical properties.

Answers to this month's crossword puzzle:

H	E	P	A	T	I	C	■	M	A	R	K	O	V	■
P	■	E	■	O	■	H	■	■	■	A	■	R	■	W
V	A	R	I	X	■	A	N	H	Y	D	R	A	S	E
G	■	C	■	I	■	R	■	I	■	I	■	L	■	I
■	B	E	H	C	E	T	■	P	O	O	L	■	K	G
S	■	N	■	■	E	■	■	■	V	■	■	S	■	H
M	E	T	A	P	L	A	S	I	A	■	C	Y	S	T
E	■	A	■	R	■	T	■	■	■	S	A	N	E	■
A	N	G	I	O	■	L	I	T	U	P	■	C	T	■
R	U	E	■	■	■	A	■	R	■	I	■	O	■	C
■	B	■	E	L	A	S	T	O	G	R	A	P	H	Y
O	■	■	■	U	■	■	■	U	■	I	■	E	A	T
S	P	L	E	N	O	M	E	G	A	L	Y	■	I	O
S	■	D	■	G	■	R	■	H	■	L	■	A	R	M
A	P	L	A	S	T	I	C	■	S	A	A	G	■	A

Interactive Crossword and Answers can also be found on our website:
www.practicalgastro.com

Posters Cited

AMERICAN COLLEGE OF GASTROENTEROLOGY ANNUAL MEETING

October 19-24, 2012, Las Vegas, NV
Orally Administered Plecanatide, A Guanylate Cyclase-C Agonist, Acts in the Lumen of the Proximal Intestine to Facilitate Normal Bowel Movement in Mice and Monkeys. (P451) Authored by Stephen Comiskey, John Foss, Gary Jacob, and Kunwar Shailubhai.

UNITED EUROPEAN GASTROENTEROLOGY WEEK

October 20-24, 2012, Amsterdam, The Netherlands
Orally Administered Plecanatide, A Guanylate Cyclase-C Agonist, Acts in the Proximal Intestine to Stimulate Fluid Secretion to Normalize Bowel Movement. (P1003)
Authored by Stephen Comiskey, John Foss and Kunwar Shailubhai.

JOINT INTERNATIONAL EUROGASTROENTEROLOGY AND MOTILITY MEETING

September 6-8, 2012, Bologna, Italy
Plecanatide, a Superior Analog of Uroguanylin, as an Oral Drug Candidate for Treatment of Gastrointestinal Functional Disorders and Diseases. (P330)
Authored by Andrea Brancale, Gary Jacob and Kunwar Shailubhai.

About Synergy Pharmaceuticals Inc.

Synergy is a biopharmaceutical company focused on the development of new drugs to treat gastrointestinal disorders and diseases. Synergy's lead proprietary drug candidate plecanatide is a synthetic analog of the human gastrointestinal (GI) hormone uroguanylin, and functions by activating the guanylate cyclase C receptor on epithelial cells of the GI tract. Synergy completed a Phase I study of plecanatide in healthy volunteers and a Phase IIa clinical trial in chronic idiopathic constipation (CIC) patients. In October, 2011, Synergy initiated dosing of patients in a major Phase II/III clinical trial of plecanatide to treat CIC. Plecanatide is also being developed to treat constipation-predominant irritable bowel syndrome (IBS-C), with the first trial in IBS-C patients planned for the second half of 2012. Synergy's second GC-C agonist SP-333 is currently in pre-clinical development to treat inflammatory bowel diseases. More information is available at:
www.synergypharma.com

About Plecanatide

Plecanatide is a member of a new class of essentially non-systemic drugs, referred to as guanylate cyclase C (GC-C) agonists, that are currently in development to treat CIC and IBS-C. Plecanatide is a synthetic analog of uroguanylin, a natriuretic hormone that regulates ion and fluid transport in the GI tract. Orally-administered plecanatide binds to and activates GC-C receptors expressed on epithelial cells lining the GI mucosa, resulting in activation of the cystic fibrosis transmembrane conductance regulator (CFTR), and leading to augmented flow of chloride and water into the lumen of the gut. Activation of the GC-C receptor pathway is believed to facilitate bowel movement as well as producing other beneficial physiological responses including improvement in abdominal pain and inflammation. In animal models, oral administration of plecanatide promotes intestinal secretion and also ameliorates GI inflammation.

Forward-Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "planned," "believe," "forecast," "estimated," "expected," and "intend," among others. These forward-looking statements are based on Synergy's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, substantial competition; our ability to continue as a going concern; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payer reimbursement; limited sales and marketing efforts and dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. There are no guarantees that future clinical trials discussed in this press release will be completed or successful or that any product will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in Synergy's Form 10-K for the year ended December 31,

2011 and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and Synergy does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

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GIVEN IMAGING REPORTS DATA SHOWING GREATER ROLE FOR CAPSULE ENDOSCOPY IN DETECTING AND MONITORING CROHN'S DISEASE

Capsule Endoscopy Found to Be Superior to Magnetic Resonance Enterography for Detecting Crohn's Disease Lesions

AMSTERDAM, THE NETHERLANDS – Given Imaging Ltd. (NASDAQ: GIVN), a world leader in GI medical devices and pioneer of capsule endoscopy, announced results of two studies suggesting an increased role for capsule endoscopy in detecting Crohn's lesions in the small bowel. The studies were presented at the United European Gastroenterology Week (UEGW), Europe's largest gastroenterology conference in Amsterdam, October 20-24, 2012.

"Capsule endoscopy for the detection of Crohn's disease in the small bowel has been clinically validated by a substantial and growing body of peer-reviewed research," said presenter Roberta Pica, M.D., Department of Clinical Sciences, Gastroenterology Unit at the Sapienza University of Rome. "As physicians, it's important to gather as much information as possible about the structural changes in the lining of the patient's small and large intestines to determine an accurate diagnosis and proper course of treatment. In this new study, early evidence shows that capsule endoscopy, widely considered the gold standard in small bowel visualization, is superior to magnetic resonance enterography (MRE) as a reliable tool to evaluate the type and extent of mucosal lesions associated with small bowel Crohn's disease. This information can lead to a more precise course of treatment with the goal to improve patient outcomes."

Dr. Pica and colleagues presented the results of a prospective study (P1414) comparing use of wireless capsule endoscopy (WCE) to magnetic resonance enterography (MRE) in the small bowel of 16 consecutive patients with confirmed or suspected Crohn's disease. In nine of 10 patients (90%), WCE detected significant lesions as indicated by the presence of erythema, aphthous, ulcers, fissures or mucosal hemorrhages, with four patients showing lesions in both the jejunum and ileum and five only of the terminal ileum. MRE was less accurate than WCE, detecting inflammatory lesions in 11 of 15 patients (73%), with two patients showing lesions in both the jejunum and ileum and nine in only the terminal ileum. In a group of nine patients who were evaluated with both examinations, WCE detected lesions in eight patients (90%), while MRE detected lesions in six (67%). In addition, 2 patients had a false negative on MRE and showed significant lesions in the terminal ileum with capsule endoscopy, and capsule endoscopy was able to exclude a false positive diagnosis of lymphoma suggested by MRE. The authors concluded that both tools are complementary methods for diagnosing small bowel Crohn's disease, noting that WCE represents a reliable tool in the evaluation of mucosal lesions for the direct visualization of the mucosal surface, while MRE enables physicians to diagnose specific alterations of the bowel wall.

Separately, Efstathios Saprikis, M.D., 2nd Department of Gastroenterology, Evangelismos Hospital, Athens, Greece, presented a poster (P0203) showing that small bowel capsule endoscopy in patients with established Crohn's disease is safe and associated with a low percentage of capsule retention. When capsule retention did occur, the majority of the cases were adequately managed with conservative treatment. Dr. Saprikis and colleagues identified 301 patients who underwent ileocolonoscopy prior to small bowel capsule endoscopy. Among the 301 eligible patients with established Crohn's disease, capsule endoscopy identified signs of Crohn's disease in the small bowel in 196 (65.1%). Capsule retention only occurred in five patients (1.66%). These reported capsule retention rates are in line with previously reported data as well as society guidelines for CE use in patients with suspected Crohn's or established Crohn's disease.

About PillCam® SB

The PillCam®SB video capsule is a minimally invasive procedure to visualize and monitor lesions

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associated with inflammatory bowel disease (IBD), Crohn's disease and obscure GI bleeding (OGIB). The PillCam measures 11 mm x 26 mm and weighs less than four grams. Now in its second generation, PillCam SB 2 contains an imaging device and light source and transmits images at a rate of two images per second generating more than 50,000 pictures during the course of the procedure. Initially cleared by the U.S. Food and Drug Administration in 2001, PillCam SB is clinically validated by more than 1,500 peer-reviewed studies. It is an accurate, patient-friendly tool used in patients two years and older by physicians to visualize the small bowel. PillCam SB is the gold standard in small bowel evaluation.

The risks of PillCam® capsule endoscopy include capsule retention, aspiration, or skin irritation. The risks of the PillCam patency capsule include capsule retention and aspiration. Endoscopic placement may present additional risks. Medical, endoscopic, or surgical intervention may be necessary to address any of these complications, should they occur.

GIVEN IMAGING REPORTS NEW STUDIES CONFIRMING CLINICAL UTILITY OF ITS FUNCTIONAL GASTROINTESTINAL DIAGNOSTICS PRODUCTS

Studies Show Value of Incorporating High Resolution Manometry in the Diagnostic Examination of Achalasia and Anorectal Disorders.

Expanding the Duration of pH Measurement Allows Doctors to Confidently Separate Healthy Patients From Those With Reflux

AMSTERDAM, THE NETHERLANDS - Given Imaging Ltd (NASDAQ: GIVN), a world leader in GI medical devices and pioneer of capsule endoscopy, announced new studies confirming the clinical utility of its functional GI products including ManoScan™ and the Bravo® pH monitoring system. The data were presented at the United European Gastroenterology Week (UEGW), Europe's largest gastroenterology conference in Amsterdam, October 20-24, 2012. Among the abstracts presented were those discussing an optimal technique for high resolution manometry (HRM), as well as data on Bravo® pH monitoring system showing that prolonged pH measurement helps predict treatment outcomes with confidence.

"These new studies indicate that the medical community continues to find additional insights to be gained through high resolution manometry and pH monitoring that will help us improve patient care," said Sabine Roman, MD, PhD., Lyon. "Different disease states, including achalasia and diabetes, cause different problems with motility. HRM allows physicians to diagnose the cause underlying the problem, which informs treatment. In addition, a new study on Bravo pH monitoring demonstrates the value of prolonged pH measurement in predicting outcomes with confidence.

Among the Studies Presented about HRM at UEG Week:

Esophageal High Resolution Manometry (HRM) in Achalasia: Evaluation of the Classification in a French Multicentric Cohort (P1562) by Sabine Roman, MD, PhD., of the Hospices Civils de Lyon, Edouard Herriot Hospital, Digestive Physiology, (Chief of department : Pr Mion), Lyon, France, and colleagues. In this study, the researchers used HRM and the Chicago Classification to evaluate and classify patients diagnosed with achalasia. They successfully classified the patients by subtype, which assisted them in drawing conclusions about the pathophysiology of the various types of achalasia.

What Diagnosis Obtained in High Resolution Manometry Depending on the Body Position Correlates Better with Gastroesophageal Reflux Assessed by pH-Metry? (P1556) by Constanza Ciriza de Los Rios, MD, of the Hospital 12 de Octubre-Gastroenterology in Madrid, Spain, and colleagues. This study focused on optimal body position for esophageal motility assessment by HRM, and aimed to determine which results obtained in HRM depending on body position predict better gastroesophageal reflux. The study authors performed HRM upright and in supine on 111 patients, all of which had double channel 24 hour-pH metry. The researchers concluded that hypotensive lower esophageal sphincter and hiatus hernia were more frequently diagnosed upright in patients with abnormal pH-metry, and thus the sitting position is better at identifying predisposing pathophysiological mechanisms of gastroesophageal reflux.

In addition, the following study was presented on Bravo® pH monitoring system:

Reflux Associated Symptoms Per Day and Symptom Index with Confidence Intervals: New Indices of Reflux-Symptom Association For Diagnosis Of Reflux Disease That Improve Prediction of Treatment Outcome From Prolonged pH-Monitoring (P0446)

by Mark Fox, MD MA MRCP, Department of Gastroenterology, Nottingham Digestive Diseases Centre, NIHR Biomedical Research Unit, Nottingham University Hospital, Queen's Medical Centre, Nottingham, United Kingdom, and colleagues. This study aimed to obtain metrics from prolonged wireless pH-studies using Bravo technology to discriminate healthy patients from those with reflux, and then predict proton-pump inhibitor (PPI) response. To accomplish this, the researchers recruited healthy volunteers and patients with reflux symptoms and assessed their symptoms with and without PPI medication. They were able to differentiate healthy volunteers from patients using Bravo pH monitoring to evaluate reflux symptoms, and concluded that prolonged pH-measurement is required to predict treatment outcomes with confidence.

About United European Gastroenterology

UEG, or United European Gastroenterology, is a professional non-profit organization combining all the leading European societies concerned with digestive disease. Together, their member societies represent over 22,000 specialists, working across medicine, surgery, pediatrics, GI oncology and endoscopy. This makes UEG the most comprehensive organisation of its kind in the world, and a unique platform for collaboration and the exchange of knowledge.

UEG's mission is continually to improve standards of care in gastroenterology, and promote ever greater understanding of digestive and liver disease -- among the public and medical experts alike. As part of that work, it runs a number of education and training courses facilitated by highly respected experts. UEG also organizes UEG Week -- the largest and most prestigious meeting of its kind in Europe. UEG Week has been running since 1992, in a variety of major cities, and now attracts more than 14,000 people from across the world. For more information, please visit www.ueg.eu

About Digestive Motility

Motility disorders occur when the natural muscle movements of the digestive tract that help to propel food content are impaired. These disorders can impact a portion or all of the digestive tract. Examples of digestive motility diseases and disorders include chronic intestinal pseudo-obstruction (CIP), gastroparesis, dysphagia, and diffuse esophageal spasm (DES).[1] Achalasia is a motility disorder that occurs when there is a complete lack of muscle movement within the esophagus, preventing food from entering the stomach. Symptoms are difficulty swallowing liquids and solids and can also include regurgitation, vomiting, weight loss, and atypical chest discomfort.[2]

About ManoScan™ ESO

ManoScan ESO is a test used to assess esophageal motor function by providing complete physiological mapping, from the pharynx to the stomach, with a single placement of a catheter. This advanced diagnostic technology allows physicians to evaluate causes of gastric reflux, difficulty swallowing, functional chest pain and pre-operative evaluations. As the first solid-state commercially available high resolution manometry technology, ManoScan™ remains the global market leader in technologically advanced solutions for assessing gastrointestinal motility. It is the only platform validated for the Chicago Classification System, the industry's standardized categorization scheme for identification of motility disorders. All ManoScan ESO systems incorporate the new ManoView ESO v 3.0.

About the Bravo® pH Monitoring System

The Bravo® pH monitoring system is the only catheter-free pH test. The procedure uses a pH capsule that is temporarily attached to the wall of the esophagus to wirelessly transmit pH data continuously for up to 96 hours. Like catheter-based pH tests, the Bravo pH Monitoring System is an ambulatory method of pH monitoring, considered the gold standard for pH measurement and monitoring of gastric reflux. The Bravo pH monitoring system collects data that are more reflective of the patient's normal daily routine to assess if the patient has GERD.

The risks of Bravo pH monitoring include: premature detachment, discomfort, failure to detach, failure to attach, capsule aspiration, capsule retention, tears in the mucosa, bleeding, and perforation. Endoscopic placement may present additional risks. Medical, endoscopic, or surgical intervention may be necessary to address any of these complications, should they occur. Because the capsule contains a small magnet, patients should not have an MRI study within 30 days of undergoing the Bravo pH test.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the

U.S. Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, projections about our business and our future revenues, expenses and profitability. Forward-looking statements may be, but are not necessarily, identified by the use of forward-looking terminology such as "may," "anticipates," "estimates," "expects," "intends," "plans," "believes," and words and terms of similar substance. Forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause the actual events, results, performance, circumstances or achievements of the Company to be materially different from any future events, results, performance, circumstances or achievements expressed or implied by such forward-looking statements. Such forward-looking statements include statements relating to the Company exploring strategic alternatives and considering possible strategic transactions involving the Company. Factors that could cause actual events, results, performance, circumstances or achievements to differ from such forward-looking statements include, but are not limited to, the ability of the Company to reach agreement on any strategic alternative and/or to complete any such alternative, as well as the following: (1) our ability to develop and bring to market new products, (2) our ability to successfully complete any necessary or required clinical studies with our products, (3) our ability to receive regulatory clearance or approval to market our products or changes in regulatory environment, (4) our success in implementing our sales, marketing and manufacturing plans, (5) the level of adoption of our products by medical practitioners, (6) the emergence of other products that may make our products obsolete, (7) lack of an appropriate bowel preparation materials to be used with our PillCam COLON capsule, (8) protection and validity of patents and other intellectual property rights, (9) the impact of currency exchange rates, (10) the effect of competition by other companies, (11) the outcome of significant litigation, (12) our ability to obtain reimbursement for our product from government and commercial payors, (13) quarterly variations in operating results, (14) the possibility of armed conflict or civil or military unrest in Israel, (15) the impact of global economic conditions, (16) our ability to successfully integrate acquired businesses, (17) changes and reforms in applicable healthcare laws and regulations, (18) quality issues and adverse events related to our products, such as capsule retention, aspiration and failure to attach or detach, bleeding or perforation that could require us to recall products and impact our sales and net income, and (19) other risks and factors disclosed in our filings with the U.S. Securities and Exchange Commission, including, but not limited to, risks and factors identified under such headings as "Risk Factors," "Cautionary Language Regarding Forward-Looking Statements" and "Operating Results and Financial Review and Prospects" in the Company's Annual Report on Form 20-F for the year ended December 31, 2011. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. Except to the extent expressly required under applicable law, the Company undertakes no obligation to release publicly any revisions to any forward-looking statements, to report events or to report the occurrence of unanticipated events.

1. http://www.agmd-gimotility.org/about_motility.htm
2. http://www.iffgd.org/site/gi-disorders/adults/motility-disorders

About Given Imaging Ltd.

Since pioneering the field of capsule endoscopy in 2001, Given Imaging has become a world leader in GI medical devices, offering health care providers a range of innovative options for visualizing, diagnosing and monitoring the digestive system. The company offers a broad product portfolio including PillCam® capsule endoscope for the small bowel, esophagus and colon. The company also offers industry-leading GI functional diagnostic solutions including ManoScan™ high-resolution manometry, Bravo® capsule-based pH monitoring, Digitrapper® pH-Z impedance, and the SmartPill® GI monitoring systems. Given Imaging is committed to delivering breakthrough innovations to the GI community and supporting its ongoing clinical needs. Given Imaging's headquarters are located in Yoqneam, Israel, with operating subsidiaries in the United States, Germany, France, Japan, Australia, Vietnam, Hong Kong and Brazil.

For more information, please visit:
www.givenimaging.com

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MEETINGS CALENDAR

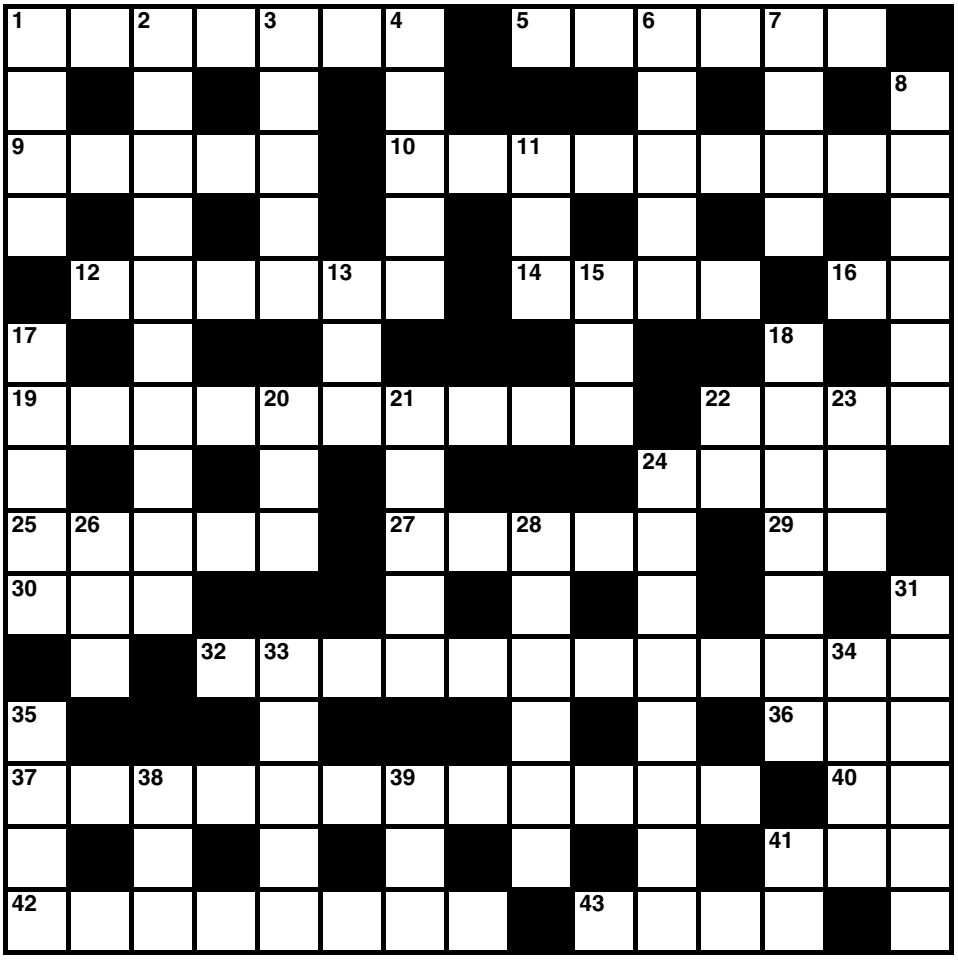
December 13-15, 2012
2012 Advances in Inflammatory Bowel Diseases, Crohn's & Colitis Foundation's Clinical & Research Conference
The Westin Diplomat, 3555 South Ocean Drive, Hollywood, FL. The premier IBD meeting of the year. Two workshops, The Future of IBD and The Basics of IBD, will be held at the conference. This "can't miss" event will inform healthcare professionals and researchers of advances and breakthroughs in the field in an effort to stimulate better care and research for patients. The outstanding faculty is comprised of expert specialists who will lead the sessions and interact with the conference attendees. For more information visit: **www.advancesinibd.com/2012/index.asp**

May 17–22, 2013
SGNA 40th Annual Course
Austin, Texas–Celebrating 40 years of Annual Course education,The Society of Gastroenterology Nurses and Associates brings together the best and brightest GI/endoscopy professionals to drive the future of our field. SGNA is the leading organization of nurses and associates dedicated to the safe and effective practice of gastroenterology and endoscopy nursing. SGNA advances the science and practice of gastroenterology and endoscopy nursing through education, research, advocacy and collaboration, and by promoting the professional development of its members in an atmosphere of mutual support. Our membership spans across the United States and 16 other countries with a full range of members from Registered Nurses, Licensed Practical/Vocational Nurses, Associates (assistants and technicians) and Advance Practice Nurses.
For more information visit: **www.sgna.org**

May 18–21, 2013
Digestive Disease Week
Orange County Convention Center, Orlando, FL. Digestive Disease Week® (DDW) is the largest and most prestigious meeting in the world for the GI professional. Every year DDW attracts approximately 15,000 physicians, researchers and academics from around the world. Choose from over 400 sessions, including clinical and research symposia, state-of-the-art lectures and research and topic fora, covering a wide array of topics and presented by a world-renowned faculty unsurpassed in their field. Try new products. DDW's exhibit hall hosts hundreds of companies showcasing the latest GI products and services.
For more information visit: **www.ddw.org**

PRACTICAL GASTROENTEROLOGY CROSSWORD PUZZLE

by Myles Mellor



ACROSS

1 The H in HVPG

5 Mathematical model used in medical studies

9 Unwanted vein

10 Enzyme that catalyzes the removal of water from a material

12 Disease also known as Silk Road, _____'s disease

14 The P in BPA

16 Kilogram, for short

19 Abnormal change of body tissue

22 Abnormal body growth

24 Sound

25 ____graphy, medical imaging technique

27 Brightened, in a way (2 words)

29 Type of scan, for short

30 Feel bad about

32 Non-invasive medical imaging technique that detects tumors

36 Erode, with away

37 Abnormal enlargemet of the spleen

40 Input/output, for short

41 Administrative branch

42 Referring to the inability of the body to create new cells

43 The value of this accurately predicts a portal hypertensive cause, abbr.

DOWN

1 Important prognostic factor in patients with cirrhosis, abbr.

2 Proportion in relation to the whole

3 Poisonous

4 Patient's record

6 The R in RFA

7 Like some vaccines

8 Patient measurement

11 Ilia location

13 Long fish

15 Female reproductive cells

17 Type of test

18 Temporary loss of consciousness caused by a fall in blood pressure

20 Expert

21 A vertebra

22 Calcium symbol

23 Rigid

24 Spirally twisted elongate rodlike bacteria

26 Key point

28 Depression

31 Sarcoma, for example

33 Breathing devices

34 Head cover

35 Bones, anatomically

38 Low-density lipoprotein

39 Diagnostic procedure, for short

41 Silver symbol

(Answers on page 70)