Gastroenterological Endoscopy (Second Edition)

Classen M, Tytgat GNJ and Lightdale C, eds
2010, Thieme, New York, NY
ISBN:978-3-13-125852-6; $299.95

This large tome, now in its second edition, is fascinating. In a field that is rapidly changing it is quite up to date with multiple references from 2008 and occasional references from 2009. It is a heavy book with thick glossy pages allowing for color photos throughout, partially explaining its high cost. I wonder if thinner pages could have decreased both the weight and the cost. The photographs are remarkable. I would prefer more arrows to highlight the areas demonstrated as this book should be available to trainees early in their careers.

The book is divided into ten sections: Development of Endoscopy; The Patient and Endoscopy; Teaching and Learning; Diagnostic Procedures and Techniques; Therapeutic Procedures; Upper GI Tract Disease; Lower GI Tract Diseases; Biliopancreatic, Hepatic, and Peritoneal Diseases; Infectious Diseases of the GI Tract; and Pediatric Endoscopy. Each section is subdivided into chapters. There is a fair amount of duplication and overlap between chapters which also lengthen the book's contents.

There are some errors that I should point out to the editors to help them with the next edition. These are relatively minor considering the volume of the book. The chapter on Patient Preparation and Assessment for Sedation (Chapter 6) is nicely done. Table 6.2 on antibiotic prophylaxis in endoscopy is unreferenced and there is no text in the chapter. The recommendation for not giving antibiotics for patients with vascular grafts is possibly correct, but it is not the current recommendation of the ASGE. In Chapter 29 the authors state "the AHA recommends antibiotic prophylaxis for all high risk patients…" The AHA discourages such antibiotic use even in dental patients 6 months following placement of a cardiac prosthesis.

The chapter on upper endoscopy recommends that at least 8 photos be taken for documentation but did not suggest a photo of the vocal cords, where possible. Eight photos seems high to me.

I have some concerns about the statement in Chapter 29 that Maloney bougies can be used with the patient in the left lateral position. Maloneys require the patient to be in the upright position to take advantage of the weight of the mercury and, unless I missed something, as they contain mercury, not tungsten.

In Chapter 14, the author comments about several reasons for not using a phosphosoda prep but does not mention the issue of renal failure. The use of a water pump and warm water to improve colonoscopy is not mentioned. I would have liked to see some discussion of split dosing for colonoscopy preparation, especially in afternoon procedures.

The chapter on Endoscopic Treatment for GERD does not mention the BARRX procedure. Chapter 38 states that some phytobezoars are treated with cellulose (instead of cellulase). Chapter 42 incorrectly describes the muscle anatomy of the esophagus

In the section on endoscopy in patients requiring anticoagulation in Chapter 7, the author recommends that "unfractionated heparin should be discontinued approximately 6 h before the procedure and LMWH should be discontinued approximately 12 h before the procedure." This recommendation is appropriately referenced. This is in agreement with the recommendation in Chapter 28. On the other hand in Chapter 14 (on colonoscopy) the author suggests heparin be stopped 3 hours before colonoscopy (unreferenced).

This is an expensive and heavy, but gorgeous, book. It probably belongs on the reference shelf of any large endoscopy unit, especially those centers with a training program.

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Capsule Endoscopy Simplified

Roberto de Franchis, Blair S. Lewis, Daniel S. Mishkin
SLACK Incorporated, 2010, 160 pp Spiral
ISBN 13 978-1-55642-940-8; $99.95

Capsule Endoscopy Simplified is an excellent beginner's guide on capsule endoscopy technology that has been rapidly gaining popularity and clinical application within adult and pediatric gastroenterology. Although the book primarily reviews technical and software capabilities of the Given Imaging (Yoqneam, Israel) Pill Cam system, it outlines features of other

currently available capsule technology designed to capture and record images of the gastrointestinal tract. It has a good balance of text, clinical pearls and images and is a valuable resource to clinical gastroenterologists in training, nurses involved with procedures, as well as more seasoned gastroenterologists who utilize this technology in patient care. This book provides a concise and thorough introduction to the equipment, patient preparation, capsule placement and software management making it a valuable reference for the endoscopy library. Throughout this book, the authors highlight a number of clinical trials in capsule endoscopy and provide evidence-based protocols in patient care. Although it does not replace an atlas of capsule images that is an essential companion to any gastroenterologist reading capsule endoscopy, it does provide a solid foundation and necessary knowledge-base to gain sufficient expertise and comfort with this technology.

This book is concise, user friendly, and offers "tricks of the trade" in addition to clinical pearls from experts in the field of capsule endoscopy and small bowel imaging. The authors provide supportive images and discussions in using this technology to diagnose various gastrointestinal diseases as well as normal and abnormal pathology.

The included DVD provides a brief overview of esophageal and small bowel video capsule endoscopy.

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Interventional and Therapeutic Gastrointestinal Endoscopy

K. Monkemuller, C.M. Wilcox, M. Munoz-Navas (editors)
Karger (2010)
ISBN: 3805593082; $248.00

This well-organized, hard cover text is designed to present "a concise yet instructive overview of the most common interventional and therapeutic GI endoscopic procedures" and is described by the editors as a "cookbook" following evidence-based medical guidelines. It consists of over 500 pages and 51 chapters covering topics ranging from anticoagulation and antibiotic prophylaxis to intraluminal stenting, ERCP, endoscopic ultrasound and endoscopic submucosal dissection. Other chapters address therapy for GI bleeding, endoscopic feeding tube placement, foreign body removal and photodynamic therapy. Chapters are authored by prominent experts but are written in a somewhat conversational tone resulting in an easy flow of high-yield information.

This book has a number of qualities that make it valuable to endoscopists and trainees. The most striking attribute to this reviewer is the large number of exhaustive tables outlining everything from antibiotic coverage for specific gastrointestinal infections, such as cholangitis and complications of esophageal perforation, to equipment specifications including outer diameter of various probes or catheters and choices of variceal band ligators or sclerosing agents. In addition to the tables, there are scores of high quality illustrations and images of GI equipment, pathology, and procedural techniques. While most of the content is evidence based, there is a fair amount of expert opinion presented. These opinions are welcome, however, as the authors are true authorities in the field, and they are accompanied by tips and tricks developed by the authors throughout their careers.

The only significant weakness of this text is the index. It is not intuitive and is somewhat limited. The table of contents is more easily used to locate specific topics, but it is not alphabetized so finding a certain

subject can be somewhat cumbersome. In addition, while the tables are tremendous, the information and specifications listed there may soon become obsolete given the rapid expansion of the therapeutic endoscopy field. Access to an online version that is updated periodically would remedy this. Online access could also provide video clips enhancing the educational value of the text.

Overall, *Interventional and Therapeutic Gastrointestinal Endoscopy* is an outstanding reference. It is practical and educational but concise enough to serve as a refresher in the minutes leading up to a difficult case. The simple but elegant images and illustrations, along with various therapeutic algorithms and endoscopic tips are quite informative. This text will be highly useful on the shelf of any endoscopy unit and valued by novice and experienced endoscopists alike.

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Hepatocellular Carcinoma: Diagnosis and Treatment (Second Edition)

Brian Carr, Ed., Humana Press
Philadelphia, PA 2009
ISBN 978-1-60327-373-2: $219.00

Hepatology has undergone a revolution in recent years. The emergence of hepatocellular carcinoma (HCC) as a significant problem in Western countries after being relegated to relative obscurity is not a minimal influence on this fact. The recent publication of *Hepatocellular Carcinoma: Diagnosis and Treatment* (Second Edition) has added a solid new tool that is well suited to clinicians who need to update their knowledge base on the modern approach to the management of this disease for the benefit of their patients. Because HCC is an entity that lends itself to multi-disciplinary management strategies, this effort incorporates a very wide cast of contributors, including hepatologists, oncologists, surgeons, radiologists, and of course, basic scientists.

Dr Carr's latest edition dedicates a full third of the total chapters to updates on epidemiology and hepatocarcinogenesis, focusing on viral, metabolic and chemical factors. It includes a fascinating chapter from NCI on genetic profiling of HCC that illustrates how modern gene array technology has advanced the targeted diagnostic and therapeutic modalities that will change how we view and treat HCC. These erudite sections help the reader to recognize the importance of mechanistic research in HCC. The textbook relies heavily in this early section to build a framework to understand how HCC management has and will continue to develop around these very important discoveries.

For the clinician who is daunted by the complex array of diagnostic and therapeutic modalities that are available today, the remainder of the book lays out the tools in detail so any gaps in knowledge can be bridged smoothly. Dr. Carr has assembled a team of experts in their respective fields who methodically outline HCC pathology, loco-regional therapies, surgical resection and liver transplantation, including the very important field of living donor liver transplantation. This segment of the book is designed to facilitate focused reading for those in need of very specific details, but it reads well as a comprehensive review for the novice.

In a very useful last chapter, Dr. Carr and two of his contributors, Drs. Marsh and Geller sum up the discipline in 2009 which is a very helpful section for the reader who needs a broad perspective before delving into more detail sections or for the novice who needs the opinion of seasoned hepato-oncologists to develop a base of knowledge. This book should find a spot with easy access in the bookshelf of a busy practicing gastroenterologist. It is a wonderful starting point for such a clinician, who may continue to see these challenging patients and needs help consolidating the modern approach.

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PEG Ifn Alpha-2A Vs. PEG Ifn Alpha-2B in Chronic Hepatitis C

A systematic review of head-to-head, randomized trials to assess the benefits and harms of the two treatments was carried out, searching the Cochrane Central Register of Controlled Trials, MEDLine, MBASE, and LILACS, and carried out through July 2009. Using standardized forms, two reviewers independently extracted data from each eligible trial report. These were statistically evaluated by combined data using a random effects meta-analysis, according to the intention-to-treat principle. Twelve randomized clinical trials were identified, including 5,008 patients that compared the two therapies.

Overall, PEG Interferon Alpha-2A significantly increased the number of patients who achieved an SVR versus PEG Interferon 2B (47% vs. 41%). Risk ration was 1.11. Subgroup analysis of risk of bias, viral genotype and treatment history yielded similar results. The meta-analysis of adverse effects leading to treatment discontinuation included 11 trials and revealed no significant differences between the two treatments.

It was concluded that current evidence suggests that PEG Interferon Alpha-2A is associated with higher SVR than PEG Interferon Alpha-2B. However, the paucity of evidence on adverse effects curves the decision to definitively recommend one treatment over the other, because any potential benefit must outweigh the risk of harm. (Awad, T., Thorlund, K., Hauser, G., et al. "PEG Interferon Alpha-2A is Associated With Higher Sustained Virological Response Than PEG Interferon Alpha-2B in Chronic Hepatitis C: Systematic Review of Randomized Trials." *Hepatology*, 2010; Vol. 51, pp. 1176-1184.)

Treatment of Collagenous Sprue

Collagenous sprue (CS) is a rare enteropathy characterized by villous atrophy and a distinctive band of subepithelial collagen that clinically includes chronic diarrhea, malabsorption and weight loss that is often unresponsive to a gluten-free diet (GFD) alone.

To evaluate the clinical characteristics, treatment, and outcomes of patients with CS, 30 patients were identified at 3 Mayo Clinic sites between 1993 and 2009 and 70% of the cohort were female, aging from 53 to 91 years. Most patients had severe diarrhea and weight loss. Hospitalization to treat dehydration was necessary in 16 (53%). Associated immune-mediated diseases were noted in 70% of the patients. Celiac disease was the most frequent.

Other associated diseases included microscopic colitis, hypothyroidism, and autoimmune enteropathy.

The median thickness of a layer of subepithelial collagen deposition in the small bowel was 29um (20 to 56.5). Subepithelial collagen deposition in the colon or stomach was noted in 8 patients. A clinical response was observed in 24 (80%) of the patients after treatment with a combination of gluten-free diet and immunosuppressive drugs. Histologic improvement was confirmed in 9 patients, with complete remission in 5 patients. Two patients died, one of complications of CS and one of another illness.

It was concluded that most patients with CS are treated effectively with a combination of gluten-free diet and steroids. (Rubio-Tapia, A., Talley, N., Gurudu, S., Wu, T., and Murray, J. "Gluten-Free Diet and Steroid Treatment Are Effective Therapy For Most Patients With Collagenous Sprue." *Clinical Gastroenterology and Hepatology*, 2010; Vol. 8, April 2010, pp. 344-349.)

Accuracy of EUS in Gastric Subepithelial Lesions

To evaluate the accuracy of EUS in diagnosing small gastric subepithelial lesions by using histology as the criterion, a retrospective study was carried out in an academic tertiary care center, including 22 patients with endoscopically resected gastric subepithelial lesions. The size, echogenicity, layer of origin and the presumptive diagnosis were determined by EUS. The diagnostic accuracy of EUS was determined by using histology as the criterion.

The mean size of the 22 lesions was 13.6 mm, with a range from 8 to 20mm. An endoscopic cap band mucosectomy device was used to resect 16 (72.7%) lesions, whereas 6 (27.3%) were resected with a saline solution-assisted and snare technique. Using histology as a criterion, the accuracy of EUS diagnosis was 10 to 22 (45.5%). EUS alone had an accuracy rate of 30.8% and 66.7%, respectively, in a diagnosis of neoplastic and nonneoplastic lesions.

It was concluded that the accuracy rate and diagnosis of subepithelial lesions was low and that endoscopic submucosal resection should be performed to provide a histologic diagnosis. Resection of small epithelial lesions of 20mm or less can be accomplished en bloc with an endoscopic cap band mucosectomy device. (Karaca, C., Turner, B., Cizginer, S., Forcione, D., Brugge, W. "Accuracy of EUS in the Evaluation of Small Gastric Subepithelial Lesions." *Gastrointestinal Endoscopy,* 2010; Vol. 71, pp. 722-727.)

Endoscopic Spray Cryotherapy for Esophageal Cancer

To assess the safety and efficacy of cryotherapy in esophageal carcinoma, a multicenter, retrospective cohort study in 10 academic and community medical centers between 2006 and 2009 was carried out in subjects with esophageal carcinoma, in whom conventional therapy failed, and those who refused or were ineligible for conventional therapy.

Treatment was considered complete when tumor eradication was confirmed by biopsy, or when treatment was halted because of tumor progression, patient preference or comorbid conditions. The study was carried out in 79 subjects with a mean age of 76%, with adenocarcinoma. Tumor stage included T1-60, T2-16, and T3-4/3.

Mean tumor length was 4 cm. Previous treatment included endoscopic resection, photodynamic therapy, esophagectomy, chemotherapy and radiation therapy that was failed in 53 patients (67%). Forty-nine completed treatment. Complete response of intraluminal disease was seen in 31 of 49 subjects (61%), including 18 of 24 (75%), with mucosal cancer.

Mean follow-up after treatment was 10.6 months overall and 11.5 months for T1 disease. No serious adverse effects were reported. Benign stricture developed in 10 (13%), with esophageal narrowing from previous endoscopic resection, radiotherapy or phototherapy noted in 9 of 10 subjects.

It was concluded that spray cryotherapy is safe and well tolerated for esophageal cancer. Short-term results suggested that it is effective in those who could not receive conventional treatment, and especially those with mucosal cancer. (Greenwald, B., Dumont, J., Abrams, J., et al. "Endoscopic Spray Cryotherapy for Esophageal Cancer: Safety and Efficacy." *Gastrointestinal Endoscopy,* 2010, Vol. 71, pp. 686-693.)

Spray Cryotherapy For Barrett's Esophagus with High-Grade Dysplasia

To assess the safety and efficacy of CRYO (cryotherapy) in Barrett's esophagus (BE) with high-grade dysplasia (HGD) in a multicenter, retrospective cohort study in 9 academic and community centers from 2007 to 2009, 98 subjects with BE and HGD with a mean length of 5.3 cm, underwent 333 treatments (3.4 treatments per subject). There were no esophageal perforations. Strictures developed in 3 subjects. Two subjects reported severe chest pain managed with oral narcotics. One subject was hospitalized for bright red blood per rectum.

Six subjects had completed all planned CRYO treatments and were included in the efficacy analysis. A total of 58 subjects (97%), had complete eradication of HGD and 52 (87%), had complete eradication of all dysplasia with persistent nondysplastic intestinal metaplasia, and 34 (57%), had complete eradication of all intestinal metaplasia. Subsquamous BE was found in 2 subjects (3%).

In this nonrandomized, respective study with no control group and a short followup (10.5 months), with a lack of centralized pathology and use of surrogate outcome for decreased cancer risk, it was concluded that CRYO is a safe and well-tolerated therapy for BE and HGD, and is highly effective in eradicating HGD. (Shaheen, N., Greenwald, B., Peery, A., et al. "Safety and Efficacy of Endoscopic Spray Cryotherapy for Barrett's Esophagus With High-Grade Dysplasia." *Gastrointestinal Endoscopy,* 2010; Vol. 71, pp. 680-685.)

Murray H. Cohen, D.O., editor of "From the Literature" is a member of the Editorial Board of *Practical Gastroenterology.*

Capsule Endoscopy in Patients with Cystic Fibrosis

Cystic fibrosis (CF) is a multi-organ disease and is associated with various GI symptoms such as abdominal pain, nausea, and constipation. Certain gastrointestinal diseases, such as distal intestinal obstruction syndrome (DIOS), are often encountered in the CF population. However, small bowel mucosal disease has not been well described. The authors of this study used wireless capsule endoscopy (WCE) to evaluate for the presence of mucosal changes in pediatric and adult CF patients. All study subjects patients also underwent fecal calprotectin testing to evaluate for intestinal inflammation.

A total of 41 CF patients (65% male with a mean age of 22 years) were evaluated by WCE, and 28 of the patients had pancreatic insufficiency. Observed lesions were categorized by the Maiden classification system. Small bowel changes, including villous damage, edema, erythema, and mucosal breaks were seen in 63% of patients, and most of the patients with lesions had pancreatic insufficiency. No correlation was seen between CF genotype and WCE findings; however, patients with pancreatic insufficiency were more likely to have mucosal changes. Additionally, fecal calprotectin levels were elevated in those patients with PI (mean 257.7 μg/g). The authors also compared the CF patients to a control group of patients who underwent WCE for other reasons, and the control group of had less severe lesions with normal fecal calprotectin levels.

The authors conclude that CF can be associated with a "CF enteropathy" which may be multifactorial in etiology, including use of pancreatic enzyme replacement therapy, intestinal dysmotility, bacterial overgrowth, change in the intestinal microbiome, or some other factor. Further studies are necessary to explain these clinical findings. (Werlin S, Benuri-Silbiger I, Kerem E, Adler S, Goldin E, Zimmerman J, Malka N, Cohen L, Armoni S, Yatzkan-Israelit Y, Bergwerk A, Aviram M, Bentur L, Mussaffi H, Bjarnasson I, Wilschanski M. "Evidence of intestinal inflammation in patients with cystic fibrosis." *Journal of Pediatric Gastroenterology and Nutrition.* 2010; 51: 304-308).

Probiotics and Colic

Infantile colic is a frustrating condition for both parents and the treating physician. The cause of this condition is unknown although increase in certain types of bacterial flora, such as *Escherichia coli*, has been noted in some infants with colic. The authors of this study evaluated the addition of the probiotic, *Lactobacillus reuteri* DSM 17938, to the diet of infants with colic.

The strength of this study was that it was randomized, double-blinded, and placebo-controlled. Infants with colic received either *L. reuteri* DSM 17938 or placebo at a dosage of 5 drops once daily for 21 days. Surveys were given to parents to assess for clinical characteristics of the study infants, and fecal samples were obtained at enrollment and on the last day of treatment for microbiologic analysis.

In total, 50 infants were randomly assigned to either receive probiotic or placebo (25 patients in each arm). There was no significant difference between the two groups in mode of delivery, gender, age at study entry, family history of gastrointestinal disease, breast feeding, or growth. There was a significant decline in daily crying time in the infants receiving probiotic at the end of the study but not before study conclusion. Also, infants receiving the probiotic had a higher clinical response (defined as a 50% reduction in crying time from baseline) at 7 days, 14 days, and 21 days of receiving the intervention. Fecal microflora showed changes as well. Infants receiving the probiotic had higher levels of *L. reuteri* DSM 17938 and and lower levels *E. coli* by the end of the study. Patients receiving the probiotic also had a significant decrease in the fecal ammonia levels.

This study demonstrates that *L. reuteri* DSM 17938 may be an effective therapy for treatment of infant colic. Likewise, bacterial overgrowth of coliforms may contribute to colic. Although this is a well-designed study, further safety studies are needed to determine the effectiveness and safety of probiotics in the treatment of infantile colic. (Savino F, Cordisco L, Tarasco V, Palumeri E, Calabrese R, Oggero R, Roos S, Matteuzzi D. "*Lactobacillus reuteri* DSM 17938 in infantile colic: a randomized, double-blind, placebo-controlled trial." *Pediatrics*. 2010; 126: e526-e533).

Survival After Pediatric Intestinal Transplant

Intestinal transplantation often is considered in the pediatric patient who has intestinal failure but has progressive

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clinical deterioration despite parenteral nutrition. The authors of the study utilized the United Network of Organ Sharing (UNOS)/Organ Procurement and Transplantation Network (OPTN) to evaluate pediatric patients listed for intestinal transplantation over a 17-year period (1991–2008). Patients were separated based on their underlying disease and were further defined as two large groups including "short gut syndrome" (including gastroschisis, intestinal volvulus, necrotizing enterocolitis, intestinal atresia, or some other type of mass intestinal resection) and "functional bowel problem" (including Hirschsprung disease and other functional short bowel diseases, such as microvillous inclusion disease).

A total of 852 children received an intestinal transplant during this time period, and the median age at the time of transplant was one year. The most common disease at the time of transplant listing was gastroschisis (24% of patients). Concomitant liver transplantation occurred in 70% of these patients. The disease group more likely to receive a liver transplant with intestinal transplantation included patients with necrotizing enterocolitis (90% of these patients).

A Kaplan-Meier survival curve demonstrated that 73% of patients were alive at one year, and 55% were alive at 5 years. Survival was higher in patients who had surgery after 2002. Patients with isolated intestinal transplantation had a better survival than patients with combined intestinal/liver transplantation. Additionally, survival appeared to be dependent on the underlying cause of disease. For example, long-term survival was highest for children with intestinal volvulus but was lowest for children with Hirschsprung disease.

This study is the largest retrospective study to date evaluating long-term intestinal transplant patient survival, and the authors have found possible predictive factors for survival. The increased survival noted over the study time period also suggests improvement in surgical technique and immune suppression in this patient population. (Lao O, Healey P, Perkins J, Horslen S, Reyes J, Goldin A. "Outcomes in children after intestinal transplant." *Pediatrics*. 2010; 125: e550-e558).

Severe Ulcerative in Children

As in adults, ulcerative colitis (UC) in children can become very severe and have no response to standard intravenous glucocorticoid therapy. However, it is difficult to follow long-term data on the sickest of these patients due to the rare nature of this disease. Data was provided from several academic children's hospitals to provide a prospective multicenter study called "Outcome of Steroid Therapy in Colitis Individuals." This study looked at short-term corticosteroid response rates in pediatric patients with UC and followed this patient group for one year to see if other medical therapy, such as biologic agents, were needed for disease control. Disease activity was monitored using the PUCAI (Pediatric Ulcerative Colitis Activity Index) as well as other laboratory markers, including a complete blood count, erythrocyte sedimentation rate, C-reactive protein level, serum albumin, and fecal calprotectin. Patients were considered steroid dependent if they received steroids for at least 6 months. All data was sent to a coordinating site for analysis.

A total of 128 patients were treated with intravenous corticosteroids of which 91 (71%) responded clinically. However, of the remaining 37 steroid nonresponders (29%), 1 received cyclosporine, 3 underwent colectomy, and 33 received infliximab. The study noted that 25 (76%) receiving infliximab improved to either clinical remission or mild disease. Younger patients, patients with new-onset disease, and patients with less severe disease (determined by PUCAI) were more likely to respond to steroid therapy. Additionally, a calculated PUCAI at day 3 and 5 of steroid therapy was able to accurately identify those patients requiring additional therapy as described above.

This study demonstrates that the PUCAI can identify those patients with UC that will require additionally therapy besides standard steroid use. Also, this study demonstrated the efficacy of infliximab therapy for those pediatric UC patients not responding to steroids. (Turner D, Mack D, Leleiko N, Walters T, Uusoue K, Leach S, Day A, Crandall W, Silverberg M, Markowitz J, Otley A, Keljo D, Mamula P, Kugathasan S, Hyams J, Griffiths A. "Severe pediatric ulcerative colitis: a prospective multicenter study of outcomes and predictors of response." Gastroenterology. 2010; 138: 2282-2291).

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Gore Delivers New Choice for Complex Soft Tissue Reinforcement

Economical Alternative to Biologics, Now In Larger Sizes

W. L. Gore & Associates (Gore) announced the availability of larger sized GORE® BIO-A® Tissue Reinforcement, a valuable alternative to biologics for reinforcement of soft tissue in surgical procedures. GORE BIO-A Tissue Reinforcement is a unique non-biologic scaffold that is gradually absorbed by the body. The open, highly interconnected 3D pore structure facilitates rapid cell infiltration and vascularization.

Since GORE BIO-A Tissue Reinforcement is not derived from biologic tissue; there is no risk of disease transfer like those associated with human or animal tissue. Due to the synthetic nature of GORE BIO-A Tissue Reinforcement, surgeons see an additional advantage over biologics in the product's uniformity, thickness, and consistency. Clinical evidence demonstrates that the scaffold guides regeneration of favorable type I collagen. With a three-year shelf life that requires no special handling, storage or tracking, the versatile material of GORE BIO-A Tissue Reinforcement is an easy to use, performance proven choice that offers value to surgeons and hospitals.

"The [GORE]BIO-A product is a viable alternative to biologics with comparable or even better results when used with proper abdominal wall reconstruction techniques," said Dr. Alfredo Carbonell, Chief, Division of Minimal Access and Bariatric Surgery and Co-director of the Hernia Center at Greenville Hospital System University Medical Center. "Unfortunately, the historical explosion in utilization and plethora of available biologic products has far superseded the evidence of their effectiveness. At a fraction of the cost of biologics there is a strong economic argument for the use of bioabsorbables, like the BIO-A material."

"Our clinical data suggests surgeons may want to consider using the BIO-A material for soft tissue reinforcement," said Dr. Garth Jacobsen, Director of the University of California, San Diego, Hernia Center. "The BIO-A product will perform at least as well, if not better, than a biologic when used appropriately, and has the absolute benefit of a significantly reduced cost profile. The ease of use is an added advantage to the surgeon."

"At Gore Medical, we have a long track record of providing safe and valuable options to physicians and patients. GORE BIO-A Tissue Reinforcement is one more way in which we are changing the landscape," said Ron Anderson, associate with the General Surgical Products Business for Gore Medical.

GORE BIO-A Tissue Reinforcement is intended for use in the reinforcement of soft tissue, including hernia repair (in non-load bearing applications), muscle flap reinforcement and general tissue reconstructions. More specific applications include: stoma reversal, paraesophageal/hiatal hernia repair, breast reconstruction using pedicled TRAM flap, abdominoperineal resection and abdominal wall reconstruction. For more information, visit www.goremedical.com.

Two Pivotal Vectibix® Phase 3 Studies in First and Second-Line Treatment of Metastatic Colorectal Cancer Published in the *Journal of Clinical Oncology*

Amgen announced that results from the PRIME '203' and '181' pivotal Phase 3 trials evaluating Vectibix® (panitumumab) in combination with chemotherapy (FOLFOX or FOLFIRI) as a first and second-line treatment for metastatic colorectal cancer (mCRC), respectively, were published online in the *Journal of Clinical Oncology.*

"Both studies demonstrated that Vectibix administered with chemotherapy significantly improved progression-free survival in patients with wild-type KRAS mCRC," said Marc Peeters, M.D., Ph.D., Professor of Oncology, Antwerp University Hospital and '181' trial lead investigator and study author. "The adverse event profiles in both trials were as expected for an anti-EGFR antibody treatment used in combination with these types of chemotherapy regimens. Additionally, these data reinforce that KRAS status should be known when choosing treatment strategies."

PRIME '203' Results in First-Line mCRC Demonstrate Vectibix Combined with Chemotherapy (FOLFOX) Helped Patients with Wild-type KRAS mCRC Live Longer Without their Disease Worsening (Progression-Free Survival or PFS)

The addition of Vectibix to FOLFOX (an oxaliplatin-based chemotherapy) significantly improved PFS (median 9.6 months for Vectibix plus FOLFOX versus 8.0 months for patients treated with FOLFOX alone, hazard ratio 0.80; 95 percent CI: 0.66–0.97; p = 0.02) in the first-line treatment of patients with wild-type KRAS mCRC.

Although numerically greater (23.9 months versus 19.7 months, hazard ratio 0.83; 95 percent CI: 0.67–1.02), the improvement in overall survival (OS) (secondary endpoint) in the Vectibix arm did not achieve statistical significance (p = 0.072) in the same patient population.

Importantly, in patients with tumors harboring activating KRAS mutations, PFS was significantly inferior in the Vectibix arm. For patients with mutant KRAS tumors, median PFS was 7.3 months with Vectibix in combination with FOLFOX versus 8.8 months with FOLFOX alone (hazard ratio 1.29; 95 percent CI: 1.04–1.62; p = 0.02).

These data confirm previous findings when oxaliplatin-based chemotherapy and an anti-EGFR antibody were combined in patients bearing tumors with activating KRAS mutations.

The response rate of Vectibix plus chemotherapy was higher than chemotherapy alone in the wild-type KRAS patient population as measured by blinded central review (55 percent versus 48 percent in the FOLFOX only arm).

Tumor KRAS status was ascertained in 93 percent of the 1,183 patients enrolled in the PRIME '203' trial, the highest number ever prospectively reported for a first-line trial.

"The outcome of this high quality trial demonstrated that Vectibix, which was administered every two weeks, improved progression-free survival as a first-line metastatic colorectal cancer treatment in a selected patient population," said Jean Yves-Douillard, M.D., Ph.D., director Clinical and Translational Research, Medical Oncology Branch, Centre R Gauducheau, France and PRIME '203' trial lead investigator and study author.

'181' Results in Second-Line mCRC Demonstrate Vectibix Combined with Chemotherapy (FOLFIRI) Helped Patients with Wild-type KRAS mCRC Live Longer Without their Disease Worsening (PFS)

Results of the '181' trial showed that the addition of Vectibix to FOLFIRI (an irinotecan-based chemotherapy) significantly improved PFS (co-primary endpoint) (median 5.9 months for Vectibix plus FOLFIRI versus 3.9 months for patients treated with FOLFIRI alone, hazard ratio 0.73; 95 percent CI: 0.59–0.90; p = 0.004) in the second-line treatment of patients with wild-type KRAS mCRC.

Although numerically greater (median 14.5 months versus 12.5 months; hazard ratio 0.85; 95 percent CI: 0.70–1.04), the improvement in overall survival (co-primary endpoint) in the Vectibix arm did not achieve statistical significance (p = 0.12) in the same patient population.

The addition of Vectibix to chemotherapy in the '181' trial resulted in greater than a three-fold improvement (35 percent versus 10 percent) in response rate in the wild-type KRAS patient population, as measured by a blinded central review.

Tumor KRAS status was ascertained in 91 percent

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of the 1,186 patients enrolled in the '181' trial, the highest number ever prospectively reported for a second-line trial.

In this study, the addition of Vectibix had no positive or negative effect on PFS or OS in patients with tumors harboring activating KRAS mutations.

"The response rate seen in the '181' trial is among the highest ever reported in the second-line metastatic colorectal cancer setting," said Emily Chan, M.D., Ph.D., Assistant Professor of Medicine, Vanderbilt-Ingram Cancer Center and '181' study investigator and author. "Additionally, the tissue acquisition from both the '181' and '203' studies has yielded a large repository of informative data regarding the KRAS biomarker, and holds the potential of providing even more information in the future."

In general, adverse events rates were comparable across arms in both studies, with the exception of known toxicities associated with anti-EGFR therapy, such as rash, diarrhea, and hypomagnesemia. Vectibix-related grade 3/4 infusion reactions were reported in less than one percent of patients.

Originally designed to compare the treatment effect in the overall mCRC patient population, both studies were amended to analyze outcomes with respect to the presence or absence of activating mutations in KRAS in the tumor itself. These are the first Phase 3 studies to prospectively analyze the effect of an EGFR inhibitor based on KRAS status in patients with previously treated mCRC.

Results from both trials were previously presented at Europe's largest cancer conference, ECCO 15– ESMO 34, in September 2009, at the 2010 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium in January, and at the 2010 American Society of Clinical Oncology (ASCO) Annual Meeting in June.

About the PRIME '203' Trial. Patients enrolled in the '203' or PRIME trial (Panitumumab Randomized trial In combination with chemotherapy for Metastatic colorectal cancer to determine Efficacy) were randomized to receive either 6.0 mg/kg of Vectibix and FOLFOX4 once every two weeks (Q2W) or FOLFOX4 alone Q2W. The primary endpoint of the study was progression-free survival by KRAS status and secondary endpoints included overall survival, objective response rate, time to progression, duration of response and safety. Long-term follow up for overall survival is ongoing.

About the '181' Trial. The '181' trial is a global, multicenter, randomized Phase 3 study. Patients enrolled in the study were randomized to receive either 6.0 mg/kg of Vectibix and FOLFIRI Q2W or FOLFIRI alone Q2W. The co-primary endpoints were progression-free survival (which was independently tested) and overall survival. Secondary endpoints included objective response rate, time to progression, duration of response and safety by KRAS status.

About KRAS. Results from studies performed over the last 25 years indicate that KRAS plays an important role in cell growth regulation. In mCRC, EGFR transmits signals through a set of intracellular proteins. Upon reaching the nucleus, these signals instruct the cancer cell to reproduce and metastasize, leading to cancer progression. Anti-EGFR antibody therapies work by inhibiting the activation of EGFR, thereby inhibiting downstream events that lead to malignant signaling. However, in patients whose tumors harbor a mutated KRAS gene, the KRAS protein is always turned "on," regardless of whether the EGFR has been activated or therapeutically inhibited. KRAS mutations occur in approximately 40–50 percent of mCRC patients.

About Colorectal Cancer. Colorectal cancer is the fourth most common cancer in men and the third most common cancer in women worldwide. Approximately 1.2 million cases of colorectal cancer are expected to occur globally. With more than 630,000 deaths worldwide per year, it is the third leading cause of cancer-related death in the Western world. The highest incidence rates are found in Japan, North America, parts of Europe, New Zealand, and Australia, and rates are low in Africa and Southeast Asia. Rates are substantially higher in men than in women.

About Vectibix. Vectibix is the first fully human anti-EGFR antibody approved by the United States (U.S.) Food and Drug Administration (FDA) for the treatment of mCRC. Vectibix was approved in the U.S. in September 2006 as a monotherapy for the treatment of patients with EGFR-expressing mCRC after disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

The effectiveness of Vectibix as a single agent for the treatment of EGFR-expressing mCRC is based on

progression-free survival. Currently no data are available that demonstrate an improvement in disease-related symptoms or increased survival with Vectibix.

Retrospective subset analyses of mCRC trials have not shown a treatment benefit for Vectibix in patients whose tumors had KRAS mutations in codon 12 or 13. Use of Vectibix is not recommended for the treatment of colorectal cancer with these mutations.

In December 2007, the European Medicine Agency (EMA) granted a conditional marketing authorization for Vectibix as a monotherapy for the treatment of patients with EGFR-expressing mCRC with non-mutated (wild-type) KRAS after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens. Vectibix has been launched in more than 20 European Union countries, Russia, Israel, Switzerland, Australia, Canada and Japan. Applications in the rest of the world are pending. To learn more about our pioneering science and our vital medicines, visit www.amgen.com.

Recent Patient Series Demonstrates Spirus Medical's Power Spiral Endoscope Enables Unprecedented Access to GI Tract

New Technology Poised to Radically Change How GI Endoscopy is Performed

Spirus Medical, Inc. (www.spirusmed.com), a leading developer of diagnostic and therapeutic advancement systems for gastroenterology announces a series of pan-endoscopies in an average time of 60 minutes, using a flexible endoscope with an integral drive to power a single use spiral component. The initial clinical series, which was conducted outside the U.S., showed unparalleled ability to navigate the intestinal tract.

In the clinical studies, procedures were performed from a combined anal and oral route. Of the series of ten pan-endoscopies, one examined the entire small bowel from the oral route in 24 minutes; another examined the entire small bowel from the anal route in 30 minutes. Current endoscopic modalities rarely accompli sh complete GI examinations and often require several hours when they do.

"The power spiral endoscope is a truly game-changing technology that has immediate applications in how gastroenterologists evaluate intestinal disorders, with an additional range of potential applications in patients with surgically-altered anatomy—e.g., bariatric surgery, "said Dr. Oleh Haluszka, Director, GI Endoscopy at Fox Chase Cancer Center, Philadelphia. Using the powered scope for the first time, Dr. Haluszka was able to negotiate the GI tract from mouth to colon in 24 minutes.

Spirus Medical has developed the Endo-Ease® line of devices aimed at revolutionizing GI endoscopy which are extensively used today to access remote areas in the small bowel and in the colon. The power spiral endoscope is the latest innovation of the technology, which integrates the spiral mechanism directly into a flexible scope. In the study, powered spiral endoscopy demonstrated rapid and complete GI access and could give physicians the ability to diagnose and treat immediately as compared to having the patient return for multiple diagnostic and/or therapeutic procedures.

Physicians participating in the initial study believe the power spiral endoscope's ability to rapidly diagnose and treat intestinal lesions makes it a candidate to quickly supplant capsule endoscopy. The latter technology has been found to have numerous drawbacks according to the clinicians, including the fact that capsule endoscopy is often inconclusive and patients are required to undergo a second procedure for treatment if pathology is identified in the first round of examination.

"The extremely successful clinical evaluations over the last several months made it clear that we have created a powerful endoscopic tool that will be a disruptive force in the GI marketplace. It will create a paradigm shift that will change the way endoscopy is performed," said St even Tallarida, President and CEO. "Best of all, the initial response from the clinicians experienced with power spiral suggest there will be a substantial medical benefit for millions of patients worldwide."

The power spiral endoscope opportunity includes a capital equipment component (scope/light source/processor) as well as a disposable spiral component that is replaced after each use. "The power spiral can immediately capitalize on a $100 million market opportunity for the disposable spiral component alone," said Bob Ailinger, COO of Spirus. According to iData Research, projected growth in the marketplace over the next five years will create a commercial opportunity estimated at $500 million just in the small bowel segment of the overall market. ■