ASPEN ANNOUNCES PUBLICATION OF THE GUIDEBOOK ON ENTERAL MEDICATION ADMINISTRATION

- ***An essential resource for all clinicians caring for enteral nutrition patients.***
- ***Includes more than 160 drug monographs.***

SILVER SPRING, MD — The American Society for Parenteral and Enteral Nutrition (ASPEN) announced the publication of the Guidebook on Enteral Medication Administration, a critical resource for healthcare providers managing patients who receive medications through their feeding tubes.

"This Guidebook not only covers the foundational science that underpins enteral medication administration, but also includes specific recommendations for individual medications," said Peggi Guenter, PhD, RN, FAAN, FASPEN, senior director of clinical practice, quality and advocacy, ASPEN. "It pulls together available information from multiple sources into one easily accessible resource. It is the only book in the US focused on safe medication delivery via feeding tubes."

"With the ongoing ENFit® transition, all care providers need to know how to appropriately administer medications via feeding tubes. The easy-to-find information in the Guidebook can support clinicians to deliver medications safely."

Edited by Dr. Joseph Boullata, the Guidebook will be a valuable resource to pharmacists, nurses, dietitians, and physicians involved in managing enteral nutrition patients.

Part 1: Foundational Science

The first section covers enteral access devices, drug interactions with nutrition, foundational principles of drug solubility and bioavailability, and the most current recommendations for drug preparation and administration.

Part 2: Individual Drug Monographs

The second section contains more than 160 drug monographs that summarize pharmaceutical and pharmacokinetic data, review enteral administration and nutrition considerations, and include recommendations on how to prepare and administer each drug.

"A goal of mine has always been to help develop clinicians who are well grounded in science and clinical evidence, who can use this as a basis to form appropriate judgment in practice," said Dr. Boullata. "It is my hope that this Guidebook will contribute toward that goal."

For more information on the Guidebook and to see a sample monograph, visit:
Nutritioncare.org/ENMeds

About American Society for Parenteral and Enteral Nutrition

The American Society for Parenteral and Enteral Nutrition (ASPEN) is dedicated to improving patient care by advancing the science and practice of nutrition support therapy and metabolism. Founded in 1976, ASPEN is an interdisciplinary organization whose members are involved in the provision of clinical nutrition therapies, including parenteral and enteral nutrition. With more than 6,500 members from around the world, ASPEN is a community of dietitians, nurses, nurse practitioners, pharmacists, physicians, scientists, students and other health professionals from every facet of nutrition support clinical practice, research and education.

For more information about ASPEN, visit:
nutritioncare.org

MALLINCKRODT PRESENTS TERLIPRESSIN CLINICAL DATA AT THE LIVER MEETING® 2018

In Post-Hoc Pooled Analysis of North American Studies, Investigational Agent Terlipressin Associated With Improvement in Survival in Patients with Hepatorenal Syndrome Type 1 with Low Baseline Mean Arterial Pressure

STAINES-UPON-THAMES, United Kingdom, – Mallinckrodt plc (NYSE: MNK), a leading global specialty pharmaceutical company, today announced results of a pooled analysis1 of terlipressin clinical trial data in patients with hepatorenal syndrome type 1 (HRS-1) at The Liver Meeting® 2018, the annual meeting of the American Association for the Study of Liver Diseases (AASLD), held Nov. 9-13 in San Francisco.

The post-hoc pooled analysis of data from two previously completed Phase 3, randomized, double-blind, placebo-controlled studies conducted in North America showed that treatment with terlipressin was associated with improved overall

(continued on page 104)

(continued from page 102)

and transplant-free survival in HRS-1 patients with lower baseline mean arterial pressure (MAP). This effect was seen independent of HRS reversal, and may relate to a marked improvement in MAP and renal function in this patient group following administration of terlipressin.

MAP is calculated using systolic and diastolic blood pressure, and can ascertain whether there is enough blood flow, resistance and pressure to supply blood to all major organs. Low MAP is common in patients with decompensated cirrhosis and HRS-1 in the absence of overt shock, and indicates a more progressed liver disease.

Terlipressin is being investigated for the treatment of HRS-1, a rare, acute, rapidly progressing and life-threatening complication of liver cirrhosis that leads to renal failure. The safety and effectiveness of terlipressin have not yet been established by the U.S. Food and Drug Administration (FDA). There are no currently approved drug therapies for HRS-1 in the U.S. or Canada.

"Patients with HRS-1 have an extremely poor prognosis and often progress to life-threatening renal failure within days,2 and we remain committed to investigating the potential clinical utility of terlipressin for these patients," said **Steven Romano, M.D., Chief Scientific Officer and Executive Vice President, Mallinckrodt**. "This pooled analysis of data from these two previously completed Phase 3 studies of more than 300 patients provides additional insights regarding the potential effect of terlipressin on key outcomes in patients with low baseline MAP. We also continue to evaluate terlipressin in our ongoing Phase 3 trial, the CONFIRM study."

"Terlipressin Treatment Is Associated With Significantly Increased Survival in Patients With Hepatorenal Syndrome Type 1 (HRS-1) and Low Baseline Mean Arterial Pressure (MAP), Independent of HRS Reversal" – the Mallinckrodt-sponsored analysis – sought to characterize the relationship between low baseline MAP and improved survival in patients with HRS-1 treated with terlipressin in the REVERSE and OT-0401 trials, which both showed that terlipressin improved renal function when administered concomitantly with albumin compared with placebo plus albumin in patients with HRS-1 and cirrhosis. Low MAP was defined as < 65mmHg.

Study Methods

Data from the two Phase 3 studies, REVERSE and OT-0401, of 307 patients with HRS-1 were pooled and analyzed. In both studies, patients received terlipressin or placebo plus albumin intravenously every six hours for up to 14 days. This pooled analysis compared terlipressin and placebo in two groups of patients: one with MAP <65 mm Hg; and a second group with MAP ≥65 mm Hg. The analysis included an assessment of overall survival; transplant-free survival; HRS reversal, defined as serum creatinine (SCr) value of ≤1.5 mg/dl; and change in SCr from baseline through end of treatment.

Key Findings

The pooled analysis of REVERSE and OT0401 clinical data showed:

- Overall survival at 90 days in the MAP <65 mm Hg group was significantly higher among patients receiving terlipressin (17/25 [68.0%]) versus placebo (6/25 [24.0%]): survival estimate was 0.680 versus 0.209, respectively; P=.005.
- No difference in overall survival at 90 days was observed between terlipressin (66/128 [51.6%]) and placebo (72/129 [55.8%]) in the MAP ≥65 mm Hg group: survival estimate was: 0.515 versus 0.554, respectively; P=.429.
- Transplant-free survival at 90 days in the MAP <65 mm Hg group was significantly higher among patients receiving terlipressin (17/25 [68.0%]) versus placebo (7/25 [28.0%]): transplant-free survival estimate was: 0.618 versus 0.083, respectively; P=.015.
- In the MAP ≥65 mm Hg group, no difference in transplant-free survival at 90 days was observed between terlipressin (67/128 [52.3%]) and placebo (76/129 [58.9%]): transplant-free survival estimate was: 0.404 versus 0.444, respectively; P=.291.
- Rates of HRS reversal among patients receiving terlipressin were similar between the MAP <65 mm Hg and ≥65 mm Hg groups; the proportion of patients with HRS reversal in the MAP ≥65 mm Hg group was significantly higher among patients receiving terlipressin than among those receiving placebo.

- Improvement in SCr from baseline to end of treatment was significantly greater with terlipressin than with placebo in both MAP groups; however, the degree of improvement was lower in the MAP ≥65 mm Hg group.

Study Limitations

This study is a post-hoc pooled analysis of completed clinical trials. Results were based on a statistical model that was not specified before the data were seen. Appropriately designed randomized, prospective studies are needed to determine the efficacy of terlipressin in this patient population, such as the company's ongoing Phase 3 study of terlipressin in HRS-1, known as The CONFIRM Study.

Details on The CONFIRM Study can be found on:
clinicaltrials.gov

Find The Liver Meeting study abstract online (abstract #959) at:
plan.core-apps.com/tristar_aasld18/abstract/3b9b2f3af8aefb4e9fba71511d9ba603

Details on the analysis can be found on Mallinckrodt's website:
mallinckrodt.com

About Hepatorenal Syndrome Type 1

Hepatorenal Syndrome Type 1 (HRS-1) is a rare condition characterized by the development of rapid kidney failure in patients with advanced chronic liver disease.[3] HRS-1 has a very poor prognosis, with a median survival time of less than two weeks and greater than 80 percent mortality within three months.[2,4] At present, there are no approved drug therapies for HRS-1 in the U.S. or Canada.[5] The only curative treatment for the underlying end-stage liver disease (cirrhosis) is liver transplantation.[3] However, many patients will not survive long enough to receive a liver transplant.[6]

About Terlipressin

Terlipressin is a V1 selective vasoconstrictor being investigated for the treatment of HRS-1 in the U.S. and Canada. Safety and efficacy have not been established with, nor has approval been granted by regulatory authorities in either country. Terlipressin is approved for use outside the U.S. and Canada, including in Europe, Latin America, Asia and Australia.

About Mallinckrodt

Mallinckrodt is a global business that develops, manufactures, markets and distributes specialty pharmaceutical products and therapies. Areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; analgesics and gastrointestinal products.

To learn more about Mallinckrodt, visit:
mallinckrodt.com

Mallinckrodt uses its website as a channel of distribution of important company information, such as press releases, investor presentations and other financial information. It also uses its website to expedite public access to time-critical information regarding the company in advance of or in lieu of distributing a press release or a filing with the U.S. Securities and Exchange Commission (SEC) disclosing the same information. Therefore, investors should look to the Investor Relations page of the website for important and time-critical information. Visitors to the website can also register to receive automatic e-mail and other notifications alerting them when new information is made available on the Investor Relations page of the website.

Cautionary Statements Related to Forward-Looking Statements

This release includes forward-looking statements concerning terlipressin, including potential benefits associated with its use. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: satisfaction of regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues; and other risks identified and described in more detail in the "Risk Factors" section of Mallinckrodt's most recent Annual Report on Form 10-K and other filings with the SEC, all of which are available

on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

1 Pappas SC, Wong F, Escalante S, Teuber P, Jamil K. Terlipressin Treatment Is Associated With Significantly Increased Survival in Patients With Hepatorenal Syndrome Type 1 (HRS-1) and Low Baseline Mean Arterial Pressure (MAP), Independent of HRS Reversal. Presented at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) (The Liver Meeting® 2018), November 9-13, 2018, San Francisco, CA. https://plan.core-apps.com/tristar_aasld18/abstract/3b9b2f3af8aefb4e9fba71511d9ba603

2 Colle I and Laterre PF. Hepatorenal syndrome: the clinical impact of vasoactive therapy, Expert Review of Gastroenterology & Hepatology. (2018) 12:2, 173-188, DOI: 10.1080/17474124.2018.1417034.

3 National Organization for Rare Disorders. Hepatorenal Syndrome. Available at: https://rarediseases.org/rare-diseases/hepatorenal-syndrome/. Accessed October 29, 2018.

4 Gines P, Sola E, Angeli P, et al. Hepatorenal syndrome. Nature Reviews. (2018) 4:23.

5 Boyer TD, Medicis JJ, Pappas SC, et al. A randomized, placebo-controlled, double-blind study to confirm the reversal of hepatorenal syndrome type 1 with terlipressin: the REVERSE trial design. Open Access Journal of Clinical Trials 2012:4. https://www.dovepress.com/a-randomized-placebo-controlled-double-blind-study-to-confirm-the-reve-peer-reviewed-article-OAJCT.

6 Rice JB, White AG, Galebach P, et al. The burden of hepatorenal syndrome among commercially insured and Medicare patients in the United States, Current Medical Research and Opinion (2017), DOI: 10.1080/03007995.2017.1331211.

WISION AI APPLIES EXPERTISE IN MACHINE-LEARNING AND MATHEMATICAL MEDICINE TO IMPROVE POLYP DETECTION DURING COLONOSCOPY

Data published in Nature Biomedical Engineering demonstrate potential of novel algorithm to improve accuracy and effectiveness of diagnostic imaging

SHANGHAI, China, (GLOBE NEWSWIRE) -- Shanghai Wision AI Co., Ltd, a leader in developing computer-aided diagnostic algorithms and systems to improve the accuracy and effectiveness of diagnostic imaging, announced results of a study validating a novel machine-learning algorithm that improves detection of adenomatous polyps during colonoscopy. Researchers at Wision AI conducted the study in collaboration with clinicians at the Center for Advanced Endoscopy at Beth Israel Deaconess Medical Center (BIDMC), Harvard Medical School and the Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, and the results appear in the current issue of ***Nature Biomedical Engineering.*** Built on the same network architecture used to develop self-driving cars, the Wision AI algorithm is designed to enable "self-driving" in colonoscopy procedures.

"Previous studies have shown that every one percent increase in the rate of detecting precancerous polyps results in a three percent decrease in the risk of interval colon cancer," said Tyler Berzin, MD, Co-Director, GI Endoscopy, and Director, Advanced Endoscopy Fellowship at BIDMC and Assistant Professor of Medicine at Harvard Medical School. "This underscores the importance of accurate polyp detection. The encouraging results obtained using Wision AI demonstrate that a novel deep-learning algorithm can automatically detect polyps during colonoscopy, opening new doors to increasing the effectiveness of screening colonoscopy and enabling a new quality control metric that may improve endoscopy skills."

"Every one percent increase in the rate of detecting precancerous polyps results in a three percent decrease in the risk of interval colon cancer," said Tyler Berzin, MD, Co-Director, GI Endoscopy.

Detecting and removing precancerous polyps during colonoscopy is the gold standard in preventing colon cancer, a leading cause of cancer death. However, the adenoma miss rate among the more than 14 million colonoscopies performed in the United States each year is 6 – 27 percent. The inability to recognize polyps within the visual field is a key reason that precancerous polyps go undetected. Studies show that having a second set of eyes on the monitor during colonoscopy procedures can increase detection rates by up to 30 percent. The Wision AI algorithm can serve as this second view by highlighting polyps directly on the monitor.

A key challenge in developing AI-based algorithms for use in clinical settings is that the dataset used to validate the algorithm is typically very small compared with the development dataset. This can result in "over-fitting" of the algorithm in a manner that limits its efficacy in real-world clinical scenarios. Additionally, in most cases, a single dataset is collected and divided for both training and validation, which may result in

(continued on page 108)

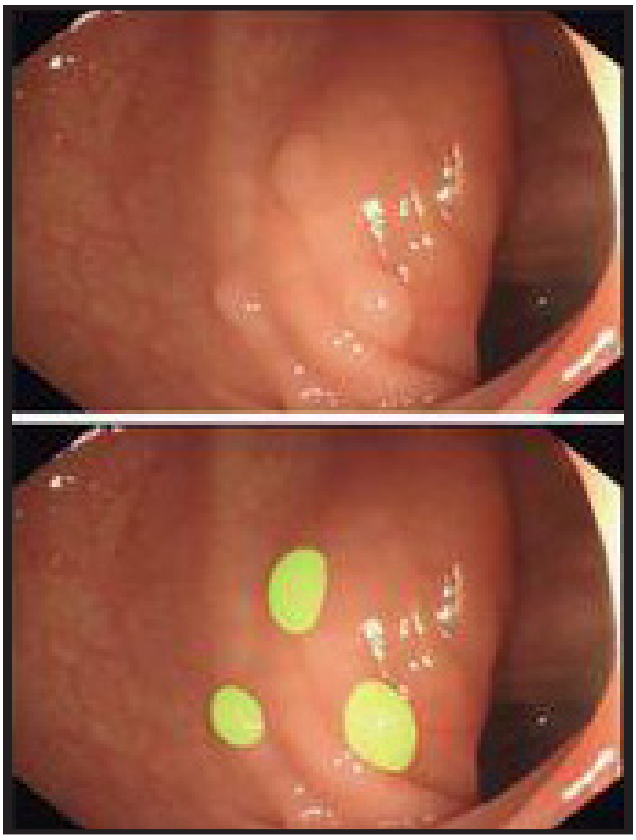
(continued from page 106)

similar data being used for both steps and therefore reducing the rigor of the validation process. In contrast, the Wision AI algorithm was validated on large, prospectively developed datasets that were collected independently from the training dataset and were several-fold larger than the training dataset. This more rigorous validation approach that Wision AI utilizes is designed to increase the performance of the algorithm in real-world clinical settings.

The algorithm was developed using 5,545 images (65.5 percent containing polyps and 34.5 percent without polyps) from the colonoscopy reports of 1,290 patients. Experienced endoscopists annotated the presence of polyps in all images used in the development dataset, and the algorithm was then validated on four independent datasets: two sets for image analysis (A and B) and two sets for video analysis (C and D).

Key findings from the study include:

- Validation on dataset A, which included 27,113 images from patients undergoing colonoscopy at the Endoscopy Center of Sichuan Provincial People's Hospital, found a per-image-sensitivity of 94.4 percent and a per-image-specificity of 95.9 percent.
  - The per-image-sensitivity in a subset of 1,280 images with polyps that are typically hard to detect was 91.7 percent.
- Validation on dataset B, based on a public database of 612 colonoscopy images acquired from the Hospital Clinic of Barcelona, found a per-image-sensitivity of 88.2 percent. The use of this dataset allowed for generalization of the validation data to a broader patient population.
- Validation on dataset C included a series of colonoscopy videos containing 138 polyps, found a per-image sensitivity of 91.6 percent among 60,914 frames of video, and a per-polyp sensitivity of 100 percent.
- Validation on dataset D, which contained 54 colonoscopy videos without any polyps, found a per-image-specificity of 95.4 percent among 1,072,483 frames.
- The total processing time for each image frame was 76.8 milliseconds, including preprocessing and displaying times before and after execution of the deep-learning algorithm. Implementation in a real-time system resulted in a processing rate of 30 frames per second with Nvidia Titan X GPUs.
- The authors conclude that this automatic polyp-detection system based on deep learning has high overall performance in both colonoscopy images and real-time videos.



"Wision AI is committed to realizing the clinical value of AI and mathematical medicine in a variety of indications, including gastroenterology, ophthalmology, neurology, and radiation-based imaging," said JingJia Liu, Chief Executive Officer at Wision AI. "The results of this study demonstrate the power of our rigorous approach to developing deep-learning algorithms, which utilizes distinct datasets for training and validation and results in high levels of specificity and sensitivity that have the potential to improve diagnostic screening methods that are known to reduce disease risk, improve health outcomes and save lives."

The first clinical trial of this technology had been completed early this year, and results from

(continued on page 110)

(continued from page 108)

this study demonstrated a significantly improved adenoma detection rate (ADR) in the AI-aided group. Full results from this first clinical trial were presented at the United European Gastroenterology Week 2018 in Vienna last week by the authors of the Nature Biomedical Engineering publication, and Pu Wang, MD, a gastroenterologist at Sichuan Provincial Hospital, received the National Scholar Award for this cutting-edge research.

About Wision AI

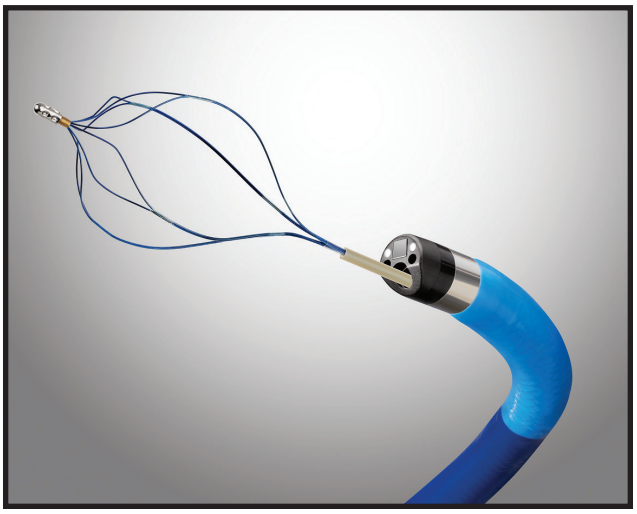
Shanghai Wision AI Co., Ltd is a leader in developing computer-aided diagnostic algorithms and systems to improve the accuracy and effectiveness of diagnostic imaging. Based in Shanghai, China, the company has extensive expertise in mathematics, algorithm development and software and hardware engineering and works closely with top-tier medical institutions in China and around the world. The company integrates medical knowledge into flexible and scalable models that leverage cutting-edge convolutional neural network and general-purpose computing to achieve high sensitivity and specificity in detection, segmentation and measurement in diagnostic imaging. Wision AI is advancing its transformative mathematical medicine approach in multiple clinical settings, including gastroenterology, ophthalmology, neurology, and radiomics.

To learn more about Wision AI, go to:
wision.com

NEWS ALERT: BOSTON SCIENTIFIC LAUNCHES NEXT-GENERATION SCOPE FOR IMPROVED ERCP VISUALIZATION

Boston Scientific launched the SpyScope™ DSII Access & Delivery Catheter, an upgraded scope for cholangiopancreatoscopy, designed to be used with the SpyGlass™ DS System to offer clearer visualization, helping physicians better identify and define bile and pancreatic duct tissue. The improved device features increased resolution and better lighting to provide physicians with clearer imaging, which may result in more efficient evaluation during cholangiopancreatoscopy.

Every year, more than one million people worldwide undergo endoscopic retrograde cholangiopancreatography (ERCP).



Cholangiopancreatoscopy may be performed during an ERCP to examine the bile and pancreatic ducts using direct visualization, which can help obtain biopsy specimens, lead to the diagnosis of abnormalities and guide stone removal.

"SpyGlass DS has been shown to provide critical diagnostic information for patients with pancreaticobiliary neoplasms, including malignancies," said Dr. Isaac Raijman, Former Chief of Gastroenterology at Baylor St. Luke's Medical Center. "In fact, a study recently published in the Journal of Clinical Gastroenterology found that 34 percent of the time, SpyGlass DS provided information that other diagnostic modalities missed that changed the treatment approach for the patient."

The company also launched two new SpyGlass DS System accessories, the SpyGlass Retrieval Basket and SpyGlass Retrieval Snare, which provide physicians with additional tools to manage difficult stones and strictures.