New Techniques Redefine Assessment of Liver Disease

Research introduces unique methods for evaluating patients with non-alcoholic fatty liver disease (NAFLD). NAFLD is the most common liver disease in the world and the development of novel procedures for definitively diagnosing the disease and assessing its prognosis is extremely important for tailoring effective treatments.

“Defeating the most common liver disease means continuing research in a field that is progressively transforming,” said Jacquelyn J. Maher, M.D., University of California, San Francisco. “The methods highlighted in these studies will permit doctors to accurately identify NAFLD and potentially predict treatment outcomes, using less invasive approaches than the current standards.”

Noninvasive Assessment of Hepatocyte Apoptosis in Nonalcoholic Fatty Liver Disease: A Multicenter Validation Study

While a liver biopsy is the standard method of diagnosis and disease progression for non-alcoholic steatohepatitis (NASH), the most extreme form of nonalcoholic fatty liver disease (NAFLD), researchers previously demonstrated that a less invasive blood test to determine caspase three-generated cytokeratin 18 fragment levels (a noninvasive biomarker test, CK-18) can predict the incidence and magnitude of NASH. A study conducted by researchers at the Cleveland Clinic in Ohio validates the utility of this novel biomarker for NASH diagnosis and assessment of disease severity in a large NAFLD population.

As an ancillary study of the NASH National Institute of Health Clinical Research Network (CRN), 178 patients with well-characterized biopsy-proven NAFLD participated in this study. Another 150 age-matched healthy controls were analyzed to validate the biomarker methodology. The team tested the NAFLD patients’ blood levels for CK-18 fragments, ranging from 68 to 3000 U/L, which were significantly higher than those observed in the 150 healthy controls (average of 45 U/L blood level).

Results reveal that accurately determining CK-18 fragment levels in the blood differentiates NASH from simple steatosis in patients with NAFLD, supporting the potential of this test in clinical practice as a noninvasive NASH biomarker. In addition to finding that CK-18 could work as a marker of NASH, the study showed that for every 50 U/L increase, the likelihood of having definitive NASH (as opposed to simple steatosis) increased by 74 percent.

“Noninvasive tools are urgently needed for the diagnosis and assessment of NASH in patients with NAFLD,” says Ariel Feldstein, M.D., of Cleveland Clinic Foundation, and co-author of this study. “This method of measuring CK-18 fragment levels in the blood may prove to be an effective noninvasive biomarker for the disease that will assist in diagnosis and prompt treatment.”

Can Phosphoproteomic Analysis of White Adipose Tissue (WAT) Predict Presence of Insulin Resistance (IR) and Resolution of Diabetes Mellitus (DM) in Non-Alcoholic Fatty Liver Disease (NAFLD)?

Diabetic patients with NAFLD are at risk for progressive liver disease. In this study, researchers examined connections between white adipose tissue (WAT, white fat) in the abdomen and medical disorders including insulin resistance (IR) and diabetes mellitus (DM) in patients with obesity and NAFLD to evaluate whether cell signaling pathway profiles within WAT are associated with the presence of IR and whether they can predict the resolution of DM after weight loss. It is important to note that some obese diabetics can completely resolve DM after weight loss.

This study, conducted by researchers at George Mason University in Fairfax, VA, included 144 patients undergoing bariatric surgery. Prior to surgery, 41 percent of these patients had evidence of IR measured by a blood test. Twenty-five percent of the 144 patients had clinically overt DM prior to surgery.

At the time of surgery, WAT was collected for protein profiling. The results were analyzed to determine whether this technique could (a) accurately predict IR in obese individuals and (b) identify which diabetic patients were destined to resolve their DM postoperatively.

Comparing patients with IR to those without IR, the phosphorylation levels of 10 proteins were significantly different between these two groups. When comparing 15 diabetics who resolved their DM after
weight loss to 10 who did not, 20 proteins were marked as significantly different between the two groups. Nearly all of these proteins are associated with insulin signaling, which leads to abnormal blood glucose levels and diabetes, leading researchers to the conclusion that “prognostic biomarkers” can be developed that can potentially predict resolution of important complications of obesity such as DM.

“Recognition of specific cell signaling pathways using Reverse Phase Protein Microarrays of WAT appears to help differentiate patients with insulin resistance from those without insulin resistance,” according to Zobair Younossi, M.D., of Inova Health System’s Translational Research Centers in Fairfax, VA, and senior author of the study. “With further confirmatory studies, this type of analysis may be effective at predicting resolution of clinically overt DM after weight-loss surgery.”

Spotlight on Liver Disease: Improving Today’s Treatments

Patients with liver disease often suffer from other related illnesses, including type-2 diabetes, obesity and high blood pressure, among others. Research explores the many unknowns of liver disease by examining new liver biomarkers, understanding disease complications and assessing novel treatments for their disease-fighting potential.

“There is still so much that researchers need to understand about the liver and its related diseases,” said Jacquelyn J. Maher, M.D., University of California, San Francisco. “Studies like these help us recognize important connections between the liver and other organs and highlight creative approaches to liver disease treatment that promise to improve the outcome of the most seriously ill patients.”

**Prediction of Coronary Atherosclerosis Disease with Liver Transaminases Level**

Recent studies have shown that non-alcoholic fatty liver disease (NAFLD) is associated with a condition known as the metabolic syndrome, which includes central obesity, type-2 diabetes, dyslipidemia and high blood pressure. However, the direct influence of NAFLD on coronary atherosclerotic disease (CAD, plaque build up in arteries) has not been investigated. This study, conducted by researchers at Isfahan University of Medical Sciences and Health Services in Isfahan, Iran, evaluated the predictive value of liver biomarkers for coronary atherosclerosis in patients with coronary heart disease (CHD).

The study enrolled 630 patients with suspicious CAD who were candidates for a coronary angiography. To assess the predictive risk of CAD, all study participants were measured for serum AST (aspartate transaminase) and ALT (alanine transaminase) concentrations—commonly measured to determine liver health—as well as C-reactive protein level and traits for metabolic syndrome.

Following the analysis, researchers found ALT and ALT/AST ratio were significantly correlated with angiographic atherosclerosis score in women (r = 0.17 and r = 0.24, respectively). Logistic regression analysis showed that ALT/AST ratio in women could predict severe CAD (OR 3.39, 95% CI 1.76–8.76). Although significant in univariate analysis, neither ALT (OR 0.98, 95% CI 0.77–1.15) nor AST (OR 0.99, 95% CI 0.72–1.22) could predict severe CAD in men.

“We found that an elevated ALT/AST ratio in women could predict coronary atherosclerotic disease that is independent of the metabolic syndrome and serum C-reactive protein concentration,” said Peyman Adibi, M.D., of Isfahan University of Medical Sciences and Health Services, and lead investigator for this study. “Therefore, further diagnostic and therapeutic interventions need to be conducted to understand the value of projecting liver biomarkers in CAD patients.”

Recombinant Factor Vlla (rFVlla) for Active Variceal Bleeding in Patients with Advanced Cirrhosis: A Multicenter Randomized Double-Blind Placebo-Controlled Trial

Variceal bleeding is a severe and frequent complication of cirrhosis, a condition in which scarring and damage to the liver reduces its function. Previous studies have suggested that recombinant factor Vlla (rFVlla), an agent used to control bleeding, may reduce the number of failures and improve 24-hour bleeding control in Child-Pugh B and C-classified cirrhotic patients with variceal bleeding. Cirrhotic patients classified in class B or C under the Child-Pugh score have a one-year sur-
vival of 81 percent and 45 percent, respectively. The current trial, conducted by researchers from several European expert centers in liver disease, was aimed at determining the efficacy and safety of rFVIIa in patients with advanced cirrhosis and active variceal bleeding.

To evaluate the therapy, 256 patients with advanced cirrhosis and active bleeding from gastroesophageal varices were randomized to placebo, 600 µg/kg rFVIIa or 300 µg/kg rFVIIa. In standard treatment, study participants were given the first dose at baseline and after endoscopy; further doses were provided at two, eight, 14 and 20 hours. Researchers observed failure rates (bleeding) within 24 hours, failure to prevent clinically significantly rebleeding or death within five days. They also monitored adverse events and 42-day mortality.

While results showed that rFVIIa as a treatment option did not improve efficacy of standard treatment, the treatment-related failures were lower than expected. While there was no significant difference in five-day mortality between groups (12% in the 600 µg/kg rFVIIa group vs.13% in placebo), the 42-day mortality was significantly lower in the 600 µg/kg rFVIIa group compared with placebo (15% in the 600 µg/kg rFVIIa group vs. 29% in placebo) and deaths due to bleeding were reduced (15% in the 600 µg/kg rFVIIa group vs. 40% in placebo). In addition, adverse events were comparable between groups.

“While there was no significant difference in the primary endpoint between treatment groups, the current trial did provide insight into the potential value and function of rFVIIa,” said Flemming Bendtsen, M.D., of Hvidovre Hospital in Hvidovre, Denmark, and co-author of this study. “Subgroup analysis of the two trials of rFVIIa in variceal bleeding are planned in order to identify characteristics of patients, who in the future may potentially benefit from this treatment.”

The Hepatitis C Link: Diagnose, Treat, Transplant
Examining Gene Expression, Drug Compounds and Liver Transplantation

Hepatitis C not only affects more than 3.9 million Americans, but continues to impact and influence the occurrence of related inflammatory conditions. Research analyzes advancements in the diagnosis of hepatitis C and therapies available to patients who suffer from the disease.

“Almost four million Americans have chronic hepatitis C infections and are at risk for of cirrhosis, liver failure, liver cancer and transplantation,” said John Vierling, M.D., Baylor College of Medicine. “These studies advance our understanding for the potential for developing markers to detect liver cancer, to increase our capacity to treat hepatitis C and provide evidence that livers from persons with hepatitis C can be successfully used for transplantation.”

Is Autotaxin (ENPP2) the Link Between Hepatitis C and Hepatocellular Cancer?

Chronic active hepatitis C (HCV) remains the strongest connection to the development of hepatocellular carcinoma (HCC, liver cancer). Unfortunately, the mechanism behind hepatitis-associated cancer remains puzzling. Such effects as oxidative stress and DNA damage are known to occur in hepatitis, through which the role of the liver in nucleic acid metabolism may be impacted. This study evaluated the key elements in nucleic acid metabolism that might account for the biologic behavior of hepatitis-associated cancer.

Autotaxin (ENPP2) is a tumor cell motility-stimulating factor and has been linked to tumor invasion and cancer growth in several human cancers, such as breast cancer and non-small-cell lung cancer. NPP2 has also been linked to adenosine triphosphate (ATP) and purinergic pathways, chemical reactions occurring within a cell to maintain homeostasis. To assess the key elements in nucleic acid metabolism, researchers looked at liver tissue collected prospectively from three patient subtypes: 1) patients undergoing liver resection for non-hepatitis related diseases; 2) HCV cancer-free transplant patients; and 3) HCV patients with biopsy-confirmed HCC.

Using microarray analysis, the group sought to profile patients with respect to cancer risk. The goal of the study was to determine whether one could identify patients at high risk for the development of cancer. Differences between groups were tested by ANOVA, a statistical test that determines the significance of any given observation.

Within purine metabolism, several genes were expressed between normal liver and both HCV groups. Of these, autotaxin was significantly elevated in

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patients with cancer compared to HCV patients without cancer or normal liver. In addition, genes associated with autotaxin, such as the lypophosphatidic acid receptor (LPA), a potent signaling molecule, were also over-expressed in HCV patients.

“Early detection of liver cancer is crucial. For patients eligible for liver transplant, early detection is associated with excellent long term cancer survival,” said Mary Maluccio, M.D., of Indiana University in Indianapolis, IN, and senior author of the study. “Autotaxin is one of the few genes within the purine metabolic pathway that is up-regulated in the liver of cancer patients versus their non-tumor bearing counterparts, and therefore may be a novel and important marker for early stage HCC in the hepatitis C-infected liver.”

**Phase II Study of Celgosivir in Combination with Peginterferon Alfa-2b and Ribavirin in Chronic Hepatitis C Genotype-1 Non-Responder Patients**

Cegsosivir is a new class of antiviral medicine in clinical development for the treatment of chronic hepatitis C virus (HCV) infection. Researchers tested this new antiviral medicine and measured its potential to offer improved treatment outcomes when combined with other anti-HCV drugs.

The current study evaluated 57 chronic HCV genotype-1 patients, separated by prior treatment status into non-responders or partial responders and randomized to three treatment groups: 1) cegsosivir 400 mg once daily in combination with peginterferon alfa-2b and ribavirin (PRC); 2) cegsosivir 400 mg once daily in combination with peginterferon alfa-2b (PC); or 3) placebo with peginterferon alfa-2b and ribavirin (PR, active control). All patients were treated for 12 weeks. The non-responders cohort enrolled 36 patients (PRC: 15; PC: 11; PR: 10) and the partial responder cohort had 21 patients (PRC: 3; PC: 9; PR: 9).

For prior non-responder patients, an Early Viral Response (EVR) was achieved in 42 percent (5/12) of those in which cegsosivir was added to the standard peginterferon alfa-2b and ribavirin therapy compared with only 10 percent (1/10) of patients receiving just peginterferon alfa-2b and ribavirin. Non-responder patient study results also demonstrate an improved mean decrease in HCV viral loads when cegsosivir is added to peginterferon alfa-2b and ribavirin of 1.63 log10 IU/mL versus 0.92 log10 IU/mL in patients treated with peginterferon alfa-2b and ribavirin alone. Eleven of the 36 non-responder patients were classified as a very difficult-to-treat patient subgroup (null responders) as they were shown to have a prior HCV treatment response of \( = 0.4 \text{log}_{10} \) to optimized therapy. In the present study, the mean decrease in HCV viral loads in these null responder patients was 1.86 log10 IU/mL with cegsosivir plus peginterferon alfa-2b and ribavirin while the two null responder patients treated with peginterferon alfa-2b and ribavirin was 0.32 log10 IU/mL. The observed difference in mean viral load between the PRC and PR treatment groups provides evidence that the combined effect of cegsosivir with peginterferon alfa-2b and ribavirin provides a clinically significant treatment benefit for difficult-to-treat chronic HCV infected patients.

“This study is the first demonstration that cegsosivir in combination with peginterferon alfa-2b and ribavirin results in a clinically significant decrease in HCV viral loads in patients highly resistant to current standard treatment,” said Kelly D. Kaita, M.D., of the University of Manitoba in Canada, and lead author of this study. “Further clinical research on the best dosing regimen and combinations is warranted to optimize the potential of this innovative combination for chronic HCV patients.”

**Use of Hepatitis C-Infected Donors in Liver Transplantation: A Case-Control Study**

To meet the increasing demand for donor livers, researchers are searching for opportunities to utilize non-optimal livers to offer some improvement to severely ill patients. Some centers are now transplanting livers from hepatitis C (HCV)-infected donors into recipients with HCV-related cirrhosis. This study compared transplant outcomes for liver recipients from HCV-infected donors to those for standard, non-extended criteria (ECD) donors to determine the possible benefits or consequences of this practice.

Researchers examined 37 recipients of livers and 76 ECD donors. Thirty percent of all donors met non-ECD criteria (standard donors) and were included as potential matches for the case-control study. Each HCV-positive liver donor recipient was matched to two standard donor recipients as matched standard
donor controls (MSDC). MSDC were classified by recipient age, primary diagnosis, cancer stage for those with HCC, recipient MELD (Model for End-Stage Liver Disease system used to prioritize waitlist patients) and donor age. Patients were monitored for graft and patient survival at three months, one year and two years; perioperative death; and HCV recurrence by four-month and one-year fibrosis (F0-F4).

In this study, researchers note that when hepatitis C positive donors were used, no difference in survival was observed. However, the rate of fibrosis appeared to be slower in those receiving HCV-infected livers. These preliminary results suggest that HCV-infected liver transplant recipients receiving livers from HCV-infected donors may have a slower rate of fibrosis progression at one year.

“This is a trend we’re seeing in survival advantage for those receiving HCV-donor grafts compared to standard donor controls,” says Paul Kwo, M.D., of Indiana University in Indianapolis, IN, and lead author of this study. “The use of HCV positive donors may be considered as a first line therapy to increase the available donor pool of organs in those undergoing OLT for HCV-related cirrhosis, which is the most common cause of cirrhosis leading to orthotopic liver transplantation. We hope to further extend this research to understand how we can maximize the use of extended criteria donor organs. This includes hepatitis C positive graft that may benefit HCV-infected individuals who require orthotopic liver transplantation, as well as gain insight as to why these organs may have a slower rate of fibrosis than non-HCV infected donor organs.”

**Could Statins Be a New Option for Hepatitis C Patients?**

Research demonstrates the potential of statins, important cholesterol management therapies, for improving the management of hepatitis C—a disease that affects nearly four million Americans. Although there have been no new treatments for hepatitis C since the introduction of pegylated interferon in 2001, the opportunity to develop a new generation of therapies that offer better outcomes may be imminent.

“Studies such as these are designed to improve the effectiveness of antivirals—the standard of care therapy for hepatitis C,” said John Vierling, M.D., Baylor College of Medicine. “The findings from these studies support the rationale and need for larger, controlled trials that may provide additional and more advantageous hepatitis C treatment options.”

**Statins Improve ALT Values in Chronic Hepatitis C Patients with Abnormal Values**

Researchers have yet to report on the concept that hepatitis C virus (HCV) patients who take statins may experience improvements in alanine transaminase (ALT, liver enzymes) levels. Use of statins for hepatitis C has not occurred in the past as the FDA-approved package insert for every statin lists “active liver disease” as a contraindication for use and hepatitis C would certainly qualify as an active liver disease. In such a setting, a researcher must request a special license form from the FDA called an investigational new drug (IND) license. As part of an IRB and FDA-approved 14-day study looking at the antiviral effect of fluvastatin (FLV) in vivo, researchers reported the total bilirubin (TB, yellow breakdown product) and ALT results and compared the findings to an existing hepatitis C registry data.

Initial results showed that three patients with abnormal ALTs at baseline experienced significant improvement and nine patients who started with normal ALTs stayed normal. In addition, there were no significant changes in TB levels. No liver problems were noted despite FLV doses that were up to four times the highest FDA-approved dose.

Experts also examined the existing HCV registry and noted both the number of patients who improved their abnormal ALT levels after statin therapy and the number of patients who maintained their normal ALT levels after initiation of statin therapy. Of the abnormal ALT group (13 of 60 pts), 12 had improved ALT and one stayed unchanged. Of the 47 beginning in the normal range, 45 maintained their ALTs. The remaining two who developed a mildly abnormal ALT after beginning a statin were noted as suffering from heavy alcohol abuse, suggesting an unrelated cause for the change.

“This is the first report of prospectively using fluvastatin in HCV patients,” says Ted Bader, M.D., of University of Oklahoma in Oklahoma City, Okla., and lead author of this study. “Two remarkable observations were made and data not only supports the lack of
harm in this situation, but also seems to suggest a possible salutary effect that needs further study.”

Retrospective Analysis of the Effect of Taking a Statin Along with Peginterferon and Ribavirin (PI+R) on SVR
Researchers retrospectively analyzed the effect of taking peginterferon and ribavirin (PI+R, hepatitis C treatment options) and PI+R plus a statin to measure the sustained viral response (SVR, negative virus in blood six months after the end of treatment) rate in hepatitis C patients. A modified intent to treat approach was taken to compare the therapy alone to the therapy with addition of a statin.

In this study, 104 patients taking PI+R were compared to 30 patients who took PI+R plus a statin. Almost all patients (25 of the 30) taking a statin were on simvastatin, two were on lovastatin, two were on atorvastatin and one on fluvastatin. According to study results, the patients on standard treatment achieved a 37 percent SVR rate—the highest SVR reported to date in the medical literature for a VA-based population. Having a high SVR rate means a cure is 95 percent of the time based upon long-term follow up that is greater than six months after treatment. The SVR rate for patients taking triple therapy, PI+R plus a statin, was 63 percent.

Statins appear to be associated with a higher SVR rate when added to standard PI+R therapy. Retrospective data are subject to many problems and inaccuracies and should be only used to plan prospective trials.

“It is important for statins to be studied prospectively for their effect on hepatitis C,” says Ted Bader, M.D., of University of Oklahoma in Oklahoma City, Okla., and lead author of this study. “Further study may contribute to developing a more effective outcome of treatment.”

New Prevention, Treatment Methods For Patients With Painful Bowel Inflammation

Popcorn Back on the Menu for Diverticular Disease; New Treatments for Ulcerative Colitis, Perianal Fistula
Nearly one million Americans experience some form of IBD every year, which is often chronic or recurring. Research looks at preventative measures and potential treatment options for these painful and debilitating conditions.

“Inflammatory bowel diseases are serious and complex diseases with varied preventative and treatment options, and we are pleased to see more attention directed toward improving the lives of people suffering from these conditions,” said Maria Abreu, M.D., Director, Inflammatory Bowel Disease Center, Associate Professor of Medicine, Mount Sinai School of Medicine. “The studies provide evidence that scientists are beginning to capitalize on previous research to better understand, prevent and treat intestinal inflammation.”

Can Patients with Diverticular Disease Eat Nuts, Corn and Popcorn?
Diverticulosis is a common disease of the large intestine characterized by pouches in the colon that bulge outward through weak spots in the colon musculature. These pouches can become inflamed, a complication referred to as diverticulitis, or they can bleed, often profusely. Patients with diverticulosis, particularly those who have complications, are frequently advised to avoid nuts and seeds; however, there is little evidence to support this recommendation. The aim of this study, conducted by researchers from the University of Washington School of Medicine and Harvard Medical School, was to prospectively evaluate whether nut, corn and popcorn consumption were associated with complications of diverticular disease.

From the Health Professionals Follow-up Study cohort, investigators selected 47,228 U.S. men aged 40–75 years at baseline (in 1986) and free of diverticulosis, gastrointestinal cancer and inflammatory bowel disease. Men reporting newly diagnosed diverticulosis or diverticular complications on biennial follow-up questionnaires were sent supplemental questionnaires outlining details of diagnosis and treatment. Recent consumption of nuts, corn and popcorn was determined from a validated 131-item semi-quantitative food frequency questionnaire mailed to the participants every four years. Study endpoints included diverticular bleeding and diverticulitis.

During 18 years of follow-up, researchers identified 383 cases of diverticular bleeding and 801 cases (continued on page 86)
of diverticulitis. Among men with diverticular bleeding no associations were observed for consumption of nuts, corn, popcorn or combined consumption. Again, among men with diverticulitis, no associations were found for corn consumption. However, after adjusting for other known or potential risk factors for diverticular complications, men with the highest popcorn intake (at least two times per week) had a 28 percent decrease in the risk of diverticulitis compared with men with the lowest intake (less than once per month). Similar statistically significant negative associations with diverticulitis were seen for men with the highest nut intake and the highest combined intake of nuts, corn and popcorn.

“In the past, many doctors have recommended that individuals with diverticulosis or diverticular complications avoid nuts and seeds because they believed that these foods could lodge in diverticula and incite inflammation or bleeding,” said Lisa L. Strate M.D., M.P.H., of the University of Washington Division of Gastroenterology in Seattle, Wash. and lead author of this study. “However, data from this large, prospective cohort suggest that these foods do not increase the risk of diverticular complications. In fact, frequent popcorn and nut consumption were associated with a decreased risk of diverticulitis.”

Expanded Adipose-Derived Stem Cells (Cx401) for the Treatment of Complex Perianal Fistula. A Phase II Clinical Trial

Complex anal fistulas, abnormal connections between the anal canal and the skin, is a chronic and highly debilitating condition affecting primarily young people and seriously compromising their quality of life. Management of complex fistulas is a challenge due to the limitations of current treatments, such as surgery and biological therapies, which are not satisfactory. Medical treatment (combination of antibiotics, antiseptics and anti-inflammatory drugs) only provides temporary relief and is usually not successful in clearing up the condition. Moreover, as a result of limited or aggressive surgical treatment, a dilemma stands between permanent recurrence and fecal incontinence. On the other hand, long-term efficacy of biological treatment is limited and adverse events can occur. The use of expanded adipose-derived mesenchymal stem cells (Cx401) is a novel cell therapy based on immunoregulation and cell proliferation, which helps repair damaged tissue.

In a multicenter, randomized, controlled trial, researchers from three Mayor Hospitals in Madrid, Spain and led by La Paz University Hospital, evaluated the efficacy and safety of Cx401 in 49 adult patients with complex perianal fistula from cryptoglandular diseases (conditions pertaining to the anal gland, n = 35) or Crohn’s disease (an inflammatory disease of the GI tract, n = 14). Patients received fibrin glue (biological product that can stimulate wound healing) alone or in addition to Cx401 (20 million stem cells) intraleisonally. If not healed, a second dose of fibrin glue or 40 million cells plus fibrin glue was administered. Fistula healing was evaluated at eight weeks. Healing was defined as absence of drainage (spontaneous or by gentle compression) and complete re-epithelization of the external openings. Recurrence rates and quality of life parameters were also analyzed.

This study found that the proportion of patients whose fistulas were healed was significantly higher with Cx401 (71 percent) than with fibrin glue (16 percent). Cx401 efficacy was observed in the cryptoglandular and the Crohn’s subpopulations. Very remarkably, at the one-year follow-up, the recurrence rate in the Cx401 group was only 17.6 percent and the impact of Cx401 administration on the patient’s quality of life was significant. At eight weeks after treatment, not a single adverse event related to the stem cells (Cx401) was observed.

“The safety profile of the product turned out to be very promising. We propose this strategy as a novel approach for the healing of patients with perianal fistula, a chronic and highly debilitating disease with unmet needs,” said Damian Garcia-Olmo, M.D., of La Paz University Hospital and lead author of this study. “Overall, we were able to determine that a dose of 20 to 60 million adipose-derived stem cells in combination with fibrin glue is an effective and safe treatment for complex perianal fistula.”