

# ADVANCES IN GASTROENTEROLOGY

**February 2013**  
SPECIAL EDITION

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## Dual Research Centers Lead Effort To Improve Treatment Options and Find a Cure for Hepatitis C

*Researchers at NewYork-Presbyterian Hospital are leaders in the pursuit to improve the safety and efficacy of pharmacologic treatments for hepatitis C, with the ultimate goal of identifying a cure for the disease, which affects some 4 million people in the United States and more than 200 million worldwide.*

### **The Center for the Study of Hepatitis C**

**A**t the Center for the Study of Hepatitis C, a cooperative effort between NewYork-Presbyterian/Weill Cornell Medical Center and The Rockefeller University, researchers are engaged in clinical and basic research initiatives designed to study issues such as how the hepatitis C virus (HCV) replicates and attacks the liver, how coinfection with HIV affects HCV, what special considerations are required for children with hepatitis C, the innate or adaptive immune responses required to eliminate or control infection, and the viral and host determinants that control the outcome of infection. The information gleaned from this research will be used to develop prophylactic or therapeutic vaccines, according to Ira M. Jacobson, MD, Chief, Division of Gastroenterology and Hepatology, NewYork-Presbyterian/Weill Cornell and Vincent Astor Distinguished Professor of Medicine, Weill Cornell Medical College. Additionally, the Center has taken a leadership role in multiple clinical trials of novel therapeutic approaches for the disease and established a serum and tissue bank (along with an electronic patient database) to create a repository for current and future studies of hepatitis C as well as prospective and retrospective analyses of patient management.

“The mission of the Center is to provide scientific and clinical research that advances our knowledge of hepatitis C and results in new and improved treatments for the millions of people around the world who are infected,” noted Dr. Jacobson. “Our Center spans the gamut, from world-class basic research at Rockefeller to cutting-edge clinical trials of novel therapies being offered to patients at the Hospital.”



Among the many trials performed at the Center was a recently published clinical trial assessing the use of boceprevir (Victrelis, Merck), a protease inhibitor (PI) approved by the FDA in 2011 for the treatment of hepatitis C, as part of a second-line or so-called salvage therapy regimen in patients with genotype-1 infection who had relapsed or failed to respond to initial therapy. The study found that boceprevir improved sustained virologic response (SVR), a key outcomes metric in hepatitis C treatment, when added to the current standard therapy for hepatitis C (ie, peginterferon alfa-2a plus ribavirin).

Dr. Jacobson and the Center also played a pivotal role in the clinical trials that led to the FDA's approval of telaprevir (Incivek, Vertex) in 2011. According to Dr. Jacobson, who served as principal investigator for the so-called ADVANCE trial, research conducted at the Center and other trial sites across the country found that treatment with telaprevir plus standard peginterferon alfa-2a plus ribavirin therapy led to an SVR rate of 75% for patients with hepatitis C genotype-1 infection, compared with an SVR rate of 44% for standard therapy alone. In general, Dr. Jacobson believes the introduction of the PIs telaprevir and boceprevir marks the most significant addition to the hepatitis C treatment armamentarium in more than a decade.

“The Center played an important role in the

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## Robotic Applications and Operating Room Technology Are Transforming the Post-Op Surgical Experience

**B**uilding on the concept of minimally invasive procedures, robotic surgical approaches performed at NewYork-Presbyterian Hospital are vastly improving the patient experience. Real-time imaging in the operating suite combined with continually advancing robotic systems offer the potential for greater precision with less trauma, less scarring, less blood loss, and quicker healing. Surgeons are driving the advances, and there are programs at both NewYork-Presbyterian/Columbia University Medical Center and NewYork-Presbyterian/Weill Cornell Medical Center that create an environment that encourages their rapid implementation.

“Our surgeons are the ones driving robotic applications. My goal is simply to ensure we are setting up our operating rooms [ORs] to facilitate these innovations,” said John C. Evanko, MD, MBA, who is Medical Director of Perioperative Services at NewYork-Presbyterian/Columbia and a gynecologic surgeon. Dr. Evanko—whose expertise with the da Vinci Surgical System includes a minimally invasive approach to treat uterine fibroids, as well as other gynecologic surgeries—reported that real-time imaging has been fundamental to creating the modern OR, which is capable of offering minimally invasive endovascular procedures, as well as radiologic-guided interventional, cardiothoracic hybrid, and robotic procedures.

“ORs for minimally invasive endovascular procedures provided a head start because they were set up for real-time imaging and had the structure and size to accommodate the equipment and connectivity that we need for robotic procedures,” explained Dr. Evanko, who works to assist OR innovation at NewYork-Presbyterian/Columbia. “Minimally invasive surgery overall and robotics in particular are now being used effectively across specialties, including

gynecology, urology, otolaryngology, and thoracic and general surgery.”

### Urology

In urology, Ashutosh K. Tewari, MD, led much of the pioneering work in robotics at NewYork-Presbyterian/Weill Cornell. Dr. Tewari, who is Director of the Prostate Cancer Institute and the LeFrak Center for Robotic Surgery, has performed more than 5,000 robotic-assisted urologic procedures, and is widely recognized for this work. Data from a recently published meta-analysis of 79 studies suggested robotic-assisted prostatectomies are at least as effective by essentially any measure, particularly in regard to the proportion of patients who achieve cancer-free margins, but generate fewer complications.<sup>1</sup>

“Robotic surgery was initially attractive because of the visualization,” Dr. Tewari explained. “While the precision of robotic excisions is an important advantage, the ability to visualize the anatomy in the structural context that can be lost in an open approach has been the most important attribute. There is also significantly less bleeding, which can also obscure the anatomy when performing a reconstruction.” However, other advantages, such as reduced blood loss, have followed.

The work by Dr. Tewari has greatly advanced the use of robotic procedures for a broad array of urologic surgical procedures, including resection of benign hypertrophy, and he has now assembled one of the most important facilities in the world for this approach. NewYork-Presbyterian/Weill Cornell’s LeFrak Center for Robotic Surgery has several unique features. In addition to a large endowment that has permitted the Center to upgrade imaging capabilities and to employ multiple robotic systems, a comprehensive therapeutic program includes a multidisciplinary team to focus on recovery with emphasis on sus-



taining a good quality of life.

“Robot-assisted surgery in urology is a mature platform at our Center. Our outcomes validate that this approach provides advantages over an open approach,” Dr. Tewari said.

Ketan K. Badani, MD, Director of Robotic Surgery at NewYork-Presbyterian/Columbia, leads one of the largest robotic oncology programs in urology. Aside from his novel work in improving urinary and sexual outcomes after robotic prostatectomy, his most recent breakthroughs have been in treating kidney tumors. “Our new technique, coined the FAST [for First Assistant Sparing Technique] robotic partial nephrectomy, has shown that, using the robotic platform, we can remove the tumor portion of the kidney while leaving the normal kidney that will continue to function in the body.<sup>2</sup> A major advantage to this minimally invasive approach is that we can save time during the critical

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development programs for both boceprevir and telaprevir, which have become part of standard therapy in patients with genotype-1 hepatitis C,” he noted. “The Center is also active in trials of second-generation PIs that have completed or are nearing completion of Phase III trials.

“The most dramatic development in the field of hepatitis C at present stems from the finding that the disease is curable without interferon,” he continued. “Among a number of oral antiviral agents under investigation, several combinations have shown very high rates of cure in early trials. The Center is actively involved in these studies, with a large number of patients currently on investigational oral regimens.”

### The Center for Liver Disease and Transplantation

As part of the effort to identify interferon-free approaches for the treatment of hepatitis C, the Center for the Study of Hepatitis C at NewYork-Presbyterian/Weill Cornell is partnering with the Center for Liver Disease and Transplantation at NewYork-Presbyterian/Columbia University Medical Center on research initiatives looking into the safety and efficacy of new regimens for patients who are on the waiting list to receive a transplant and those who have already received a transplant. Although peginterferon has been used widely in the treatment of hepatitis C for decades, it is an extremely toxic drug, particularly for patients with comorbid conditions—such as cirrhosis—that are common in hepatitis C. For these patients, extended use of interferon can lead to liver decompensation (in those with advanced liver disease), sepsis, and even death—all of which are undesirable outcomes. Not surprisingly, given that many drugs are metabolized via the liver, physicians treating patients with liver disease have to be particularly aware of liver toxicities and drug–drug interactions that may further compromise the organ.

“Patients with decompensated cirrhosis can’t tolerate interferon,” noted Robert S. Brown Jr., MD, MPH, Chief,

Center for Liver Disease and Transplantation at NewYork-Presbyterian/Columbia and the Frank Cardile Professor of Medicine at Columbia University College of Physicians and Surgeons. “Use of the drug over a full course of treatment, which is usually 48 weeks, can lead to liver failure, even if you cure the underlying HCV. As a result, we have a lot of patients on the transplant waiting list who we can’t even treat and attempt to clear the virus before transplant because they can’t take interferon—it would make their livers sick.”

According to Dr. Brown, initial forays into new treatment options for this subpopulation of hepatitis C patients included short-course therapy (12–14 weeks) with a low-accelerating dose regimen of peginterferon alfa plus ribavirin with one of the recently approved PIs, either telaprevir or boceprevir, up to the time of liver transplant. Although this approach was successful in many cases, they still found that only people with “relatively healthy livers” could tolerate interferon for even just 12 weeks, Dr. Brown noted.

To address this issue, the Center for Liver Disease and Transplantation has taken on a leadership role in clinical trials of a novel agent in the nucleotide class, sofosbuvir (GS-7977, Gilead). In these trials, researchers are using the new drug along with ribavirin in the treatment of hepatitis C both before and after liver transplant surgery. As the leading center for liver transplant in the United States, the Center for Liver Disease and Transplantation at NewYork-Presbyterian/Columbia is one of the leading enrollers of patients in these trials.

“One of the advantages of GS-7977 is that it is a nucleotide,” said Dr. Brown. “Unlike the PIs, which are metabolized by the liver, the new drug is excreted unchanged by the kidney. So, as long as the patient’s kidney function is good, we don’t predict any issues with toxicity. Even though we know the stakes are always higher with transplant patients, we still believe the potential benefits of this

new drug outweigh the risks.”

The Center is also involved in research efforts assessing the safety and efficacy of another new class of hepatitis C treatments, *NS5A* inhibitors. Although the exact role of *NS5A* in hepatitis C remains unknown, studies indicate the gene likely plays a role in viral replication. Dr. Brown believes these studies also might yield promising new therapeutic approaches. Unfortunately, the need for significant treatment advances for all liver diseases—including hepatitis C—has arguably never been more acute.

Thanks to an aging population and, perhaps, advances in critical care, the pool of eligible transplant donors has shrunk considerably over the past 5 years—particularly in New York, where the number of organs eligible for transplant has dropped by 20% over that time, according to Dr. Brown. As a result, the number of transplant procedures performed in the United States has declined by roughly 15% since 2007, meaning that waiting lists are longer than they have been in some time. Changes in how patients are screened for hepatitis C—the Centers for Disease Control and Prevention recently recommended a shift from risk factor–based screening to universal screening for all patients born between 1945 and 1965—may help specialists identify patients with the disease earlier, and thus earmark them for treatment earlier and hopefully decrease the demand for transplantation in the future.

“The aging population is not only affecting donors, but recipients,” noted Dr. Brown. “We are seeing older patients with hepatitis C, and more patients with comorbid conditions like cirrhosis. Ultimately, we want to get to a point where we don’t need to resort to liver transplantation, but that’s a long way off. And to get to that point, we need better treatments for diseases like hepatitis C, better treatment for patients who also have cirrhosis, and better treatments to resolve the fibrosis or scarring that occurs as a result of the virus. We’re putting a lot of effort into curing hepatitis C, and I think we’ll get there.”



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## Important news from NewYork-Presbyterian Gastroenterology.

Current research projects, clinical trials, and advances in the diagnosis and treatment of patients with gastroenterologic diseases

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portion of the procedure when the blood-flow to the kidney is stopped—ie, the warm ischemia time,” Dr. Badani said.

## Gynecology

For most of the diseases and conditions in which robotic surgery is now an alternative to an open approach, it is not yet clear whether robotic-assisted surgery necessarily yields better outcomes. This is difficult to prove because of the challenges of performing randomized trials with appropriate controls, but Dr. Evanko said that there are clear advantages for the patient in regard to recovery when robotic-assisted surgery reduces the size of incisions. In gynecology, the da Vinci Surgical System has been part of a movement to achieve minimal scarring and speedier return to normal activities after common procedures, such as hysterectomy and myomectomy.

“The published data that claim better outcomes with robot-assisted surgery are largely anecdotal and not any more compelling than the data which suggest that there are no outcome advantages,” Dr. Evanko said. “In my opinion, the jury is still out on whether these surgeries offer any significantly better clinical outcomes over conventional surgery, but the extent to which

this approach advances a minimally invasive approach and allows patients to recover more quickly is perceived by patients as a very important advantage.”

## Orthopedic, Gastrointestinal, Neurologic

At NewYork-Presbyterian/Columbia, robotic-assisted surgery is now being employed for some common orthopedic diseases, for resections of a vast array of malignancies, and for gastrointestinal diseases, including resections of the bowel. The precision of robotic-assisted surgery has long made it attractive for neurologic applications, but the expansion to such a broad array of organ systems is attributed primarily to its role in taking minimally invasive surgery to the next step. Although the laparoscope brought momentum to minimally invasive surgery, modern imaging systems allow visualization without a scope. It is a new approach that demands ORs with different capabilities.

“Imaging was once a preoperative device to plan surgery,” Dr. Evanko said. “Increasingly, imaging such as CT [computed tomography] scanning is an intraoperative tool to guide the procedure. The modern OR has to be large enough to

accommodate the imaging systems, the displays, the robotic devices, as well as the monitoring equipment that would be found in a conventional OR. This requires planning and the infrastructure that allows the OR to function efficiently.” Simply running the wires to an increasingly complex and sophisticated array of devices limits the degree to which the OR can be retrofitted as needs evolve.

“We have been deeply involved in attempting to anticipate these changes and to approach the development of a modern OR with a prospective approach. This has allowed us to stay at the front of the curve in expanding robotic-assisted surgery where it has advantages for the patient,” Dr. Evanko said.

## References

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