

## Local Consolidative Therapy Plus Immunotherapy or Targeted Agents for NSCLC

Clinical trials explore surgery/radiation plus immune checkpoint or tyrosine kinase inhibitors for metastatic non–small cell lung cancer

By Bryan Tutt

Local consolidative therapy with surgery and/or radiation has been proven to prolong survival for patients with oligometastatic (i.e., three or fewer metastases) non–small cell lung cancer (NSCLC), but whether patients with a greater metastatic burden would also benefit is not known. The answer may be found in two new clinical trials combining local consolidative therapy with novel systemic treatments to combat metastatic NSCLC.

In the two trials, patients first receive the immune checkpoint inhibitors nivolumab and ipilimumab (LONESTAR trial) or the tyrosine kinase inhibitor osimertinib (NORTHSTAR trial). Patients then are randomly assigned to receive maintenance therapy with the study drug(s) or local consolidative therapy followed by maintenance therapy.

“We’ve shown that local consolidative therapy benefits NSCLC patients with oligometastatic disease, and now we’re expanding the paradigm to include patients who have polymetastatic dis-

*A treatment plan for intensity-modulated radiation therapy targets a metastatic lesion near the rib in a patient with non–small cell lung cancer. The local consolidative therapy for this lesion and a lesion near the vertebral body was administered following front-line systemic therapy without disease progression. Image courtesy of Dr. Daniel Gomez.*

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## Local Consolidative Therapy for NSCLC

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ease,” said Daniel Gomez, M.D., an associate professor in the Department of Radiation Oncology at The University of Texas MD Anderson Cancer Center. “Our hope is that the combination of local consolidative therapy and immunotherapy or osimertinib can extend survival for patients with metastatic disease anywhere in the body.”

### Building on promising findings

Dr. Gomez and his colleagues hope that the combination of local consolidative therapy and immune checkpoint inhibitors or the third-generation EGFR (epidermal growth factor receptor) inhibitor osimertinib will extend survival for patients with metastatic NSCLC beyond what has been seen in studies of each modality separately.

The survival benefit of local consolidative therapy was demonstrated in a recent phase II trial (No. 2012-0618) in which patients with oligometastatic NSCLC received first-line therapy and were then randomly assigned to receive local consolidative therapy or maintenance therapy. The median progression-free survival duration of the patients who received local consolidative therapy (11.9 months) was significantly longer than that of patients who received maintenance therapy only (3.9 months;  $P = .0054$ ).

“This was the first randomized controlled trial to establish that local consolidative therapy slows disease progression in NSCLC patients with limited metastatic disease,” said Dr. Gomez, the trial’s principal investigator.

Immune checkpoint inhibitors also have been shown to benefit patients with metastatic disease. The PD-1 (programmed cell death protein 1) inhibitor nivolumab is approved by the U.S. Food and Drug Administration (FDA) for treating several types of cancer, including previously treated metastatic NSCLC. Furthermore, the combination of nivolumab and the CTLA-4 (cytotoxic T lymphocyte antigen 4) inhibitor ipilimumab—already approved by the FDA for treating metastatic melanoma—is under investigation for the treatment of metastatic NSCLC

**“We think treating as many lesions as possible is the key to prolonging survival for patients with metastatic NSCLC.”**

— Dr. Daniel Gomez

in a clinical trial (No. 2016-0223).

The EGFR inhibitor osimertinib has also shown promise against NSCLC. In March 2017, the FDA approved osimertinib for the treatment of patients with metastatic NSCLC and *EGFR* T790M mutations.

“One of the main gatekeepers of resistance to EGFR inhibitors is the T790M point mutation,” Dr. Gomez said. “It’s been shown that patients who develop resistance that way can then be treated with osimertinib and the disease responds.”

### New clinical trials

“The NORTHSTAR and LONESTAR trials are different from our previous trials of local consolidative therapy because we use novel agents and also because we include not just patients who have oligometastatic disease but also patients who have polymetastatic disease,” Dr. Gomez said. Both trials recently began enrolling patients with metastatic NSCLC.

### NORTHSTAR

Dr. Gomez is MD Anderson’s principal investigator of the multi-institutional NORTHSTAR trial (No. 2017-0228), which is enrolling patients with previously untreated or recurrent stage IIIB or IV NSCLC that is not amenable to potentially curative treatment. Treatment-naïve patients must have tumors that harbor an *EGFR* exon 19 deletion or L858R mutation, whereas patients with recurrent disease must have an *EGFR* T790M mutation that arose during treatment with an EGFR inhibitor such

as erlotinib, gefitinib, or afatinib. Patients previously treated with osimertinib or another third-generation tyrosine kinase inhibitor are not eligible for the trial.

All patients in the trial receive osimertinib for 6–12 weeks. Those whose disease does not progress during this induction therapy are then randomly assigned to receive osimertinib maintenance therapy only or local consolidative therapy followed by osimertinib maintenance therapy. All patients will continue the maintenance therapy until disease progression or unacceptable toxic effects occur. Dr. Gomez and his colleagues will compare progression-free survival between patients who received local consolidative therapy and patients who did not.

### LONESTAR

The LONESTAR trial (No. 2017-0311) is enrolling patients with stage IV NSCLC who are treatment naïve or have undergone one line of chemotherapy or targeted therapy. Patients whose disease is classified as adenocarcinoma must have wild-type *EGFR* and *ALK*; patients with other NSCLC subtypes do not need to be tested for *EGFR* or *ALK* status because such mutations are rare in these subtypes. Patients who have undergone systemic immunotherapy for their disease are ineligible for the trial.

All patients receive two 6-week cycles of nivolumab and ipilimumab. Then, patients whose disease has not progressed are randomly assigned to receive maintenance therapy only with nivolumab and ipilimumab or local consolidative therapy followed by maintenance therapy with nivolumab and ipilimumab. All patients will continue maintenance therapy for up to 2 years.

The principal investigator of this MD Anderson-only trial is John Heymach, M.D., Ph.D., a professor in and chair of the Department of Thoracic/Head and Neck Medical Oncology. The trial’s co-principal investigators are Dr. Gomez and Stephen Swisher, M.D., a professor in the Department of Thoracic and Cardiovascular Surgery and head of the Division of Surgery. The researchers will

compare overall and progression-free survival between patients who received local consolidative therapy and those who did not.

### Determining local consolidative therapy

In both the NORTHSTAR and LONESTAR trials, a multidisciplinary treatment team determines the approach for local consolidative therapy. Whether a patient should be treated by surgery, radiation, or both depends on tumor location and extent of disease. In most patients, the same modality is used to treat all lesions, but some patients are better suited for a hybrid approach in which some lesions are resected and others irradiated.

“Certain lesions tend to be better suited for surgery versus radiation therapy,” Dr. Gomez said. “We prefer to use surgery for lung lesions that can be resected with a lobectomy, for a single brain metastasis or a dominant brain

metastasis, and for some adrenal gland lesions that can be resected with relatively modest risk. Other metastases are generally treated with radiation.”

The surgeons and radiation oncologists use whichever surgical and radiation techniques are most likely to achieve treatment goals. Lung lesions may be resected by open thoracotomy or video- or robot-assisted thoracoscopy/laparoscopy; the goal for all resections is grossly negative surgical margins. For radiation therapy, stereotactic body radiation therapy is the most common modality used, although modalities such as intensity-modulated radiation therapy and proton therapy are available. The goal of radiation therapy is to ablate the disease.

“Whether we use surgery or radiation, the main point is to be aggressive,” Dr. Gomez said. “We think treating as many lesions as possible is the key to prolonging survival for patients with metastatic NSCLC.” ■

### FOR MORE INFORMATION

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### FURTHER READING

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To learn more about clinical trials for patients with lung cancer, visit [www.clinicaltrials.org](http://www.clinicaltrials.org).

## IN BRIEF

### CAR T Cells Elicit Durable Responses in Large B Cell Lymphoma

Axicabtagene ciloleucel (axi-cel), a chimeric antigen receptor (CAR) T cell therapy that targets CD19-expressing cancer cells, elicits durable responses in a substantial portion of patients with aggressive large B cell lymphoma, a recent multicenter phase I/II trial has shown.

In the trial, named ZUMA-1, patients with treatment-refractory large B cell lymphoma received axi-cel as a single intravenous infusion following a conditioning regimen of low-dose cyclophosphamide and fludarabine. In an analysis that included all 108 patients treated in either phase of the trial, the objective response (complete and partial responses) and complete response rates were 82% and 58%, respectively, at a minimum follow-up of 1 year. At the data cutoff date, with a median follow-up of about 15 months, 42% of patients continued to have a response, with 40% having a complete response.

Twenty-three patients who had either a partial response or stable disease at their first assessment 1 month after axi-cel treatment had complete responses that occurred as late as 15 months after treatment. The 15-month overall and progression-free survival rates were 56% and 41%, respectively. Three of the seven patients treated in phase I of the trial had ongoing complete responses 2 years after treatment.

Grade 3 or higher adverse events occurred in most patients and included fever, infections, leukopenia, thrombocytopenia, and anemia. In addition, most patients experienced cytokine release syndrome; although the majority of these patients had low-grade cases, two patients died of adverse events related to cytokine release syndrome. Many patients also experienced neurological events, which tended to appear about 5 days after treatment but resolved within about 15 days.

“We believe this is a major advance in the treatment of patients with relapsed or refractory large B cell lymphoma and is likely to save or prolong the lives of many patients,” said Sattva Neelapu, M.D., a professor in the Department of Lymphoma and Myeloma at The University of Texas MD Anderson Cancer Center. Dr. Neelapu was a co-first author of the study’s report, which was published in *The New England Journal of Medicine* (2017;377:2531–2544) and presented at the 2017 annual meeting of the American Society of Hematology. “This study demonstrated that axi-cel provides remarkable improvement in outcomes over existing therapies for these patients who have no curative options,” he said.

In October 2017, the U.S. Food and Drug Administration approved axi-cel for the treatment of relapsed or refractory diffuse large B cell lymphoma. ■

# Managing Opioid Use in Cancer Patients

## Vigilance and interventions ensure patient safety

By Bryan Tutt

Opioid abuse has been described as a crisis by public health professionals, as thousands of Americans die of prescription drug overdoses each year. In response to this crisis, in 2016 the U.S. Centers for Disease Control and Prevention (CDC) updated their pain treatment guidelines to reduce the use of opioids for chronic pain. However, these guidelines specifically excluded cancer patients because of the unique nature of cancer-related pain and because substance abuse was not believed to be prevalent in that patient population. But opioid overdoses and substance abuse problems do occur in a small subset of cancer patients, and clinicians at The University of Texas MD Anderson Cancer Center have implemented a system for detecting and managing issues that might arise from opioid abuse in cancer patients with chronic pain.

“Recent studies from our group and others show that some cancer patients who have pain and receive opioids experience problems that put them in danger of accidental overdose,” said Joseph Arthur, M.D., an assistant professor in the Department of Palliative, Rehabilitation, and Integrative Medicine. These studies led to a multidisciplinary approach to screening and intervention aimed at avoiding such issues while ensuring that patients in MD Anderson’s Supportive Care Center receive adequate treatment for their chronic pain.

“Our goal is to keep our patients safe so they can focus on fighting their cancer,” said Tonya Edwards, M.S.N., R.N., an advanced practice nurse in the Department of Palliative, Rehabilitation, and Integrative Medicine.

### Assessing patient risk

When a patient is referred to the Supportive Care Center for chronic



*Members of a compassionate high-alert team compare notes before meeting with a patient who is receiving opioids for pain. The team approach is used to ensure the safety of patients who receive opioids for cancer pain and may have opioid use disorders. From left: Dr. Suresh Reddy, assistant managing nurse Manju Joy, pharmacist EdenMae Rodriguez, advanced practice nurse Tonya Edwards, and Dr. Joseph Arthur.*

pain that requires opioids, the staff uses several tools to assess the patient’s risk of developing an opioid use disorder. First, the clinicians note any personal or family history of alcohol or drug abuse in the patient’s medical record. Next, the patient is asked to fill out two short questionnaires, the CAGE-AID (the CAGE alcohol screening questionnaire adapted to include drugs) and the SOAPP-R (Screener and Opioid Assessment for Patients with Pain–Revised), both of which are validated screening tools for drug abuse risk.

If the patient appears to be at risk, the staff may check the prescription drug monitoring program in the patient’s state of residence to see whether the patient is currently receiving or has in the past received opioids.

“These screening tools together tell us whether the patient is likely to develop an opioid use disorder,” Dr. Arthur said. He emphasized that patients found to be at high risk still receive the opioids necessary to manage their pain, but extra measures are put in place to protect the patient.

### Ensuring patient safety

Typically, when a patient requires an opioid—regardless of the patient’s risk of opioid use disorders—Supportive Care Center staff members first explain the benefits and possible adverse effects of the drug. The patient also receives information about appropriate storage and disposal of the drug. “Sometimes, especially for patients at risk of substance abuse, we use an opioid management plan,” Dr. Arthur said. “This lays



out the goals and expectations of the pain therapy and what each party—the care team and the patient—has to do. For the patient, these expectations include getting opioid prescriptions from only one doctor and one pharmacy.”

Some patients—especially those who need high doses of opioids or receive medications such as benzodiazepines that have potentially lethal interactions with opioids—are given a prescription of naloxone nasal spray for use in case of an overdose. Dr. Arthur and his colleagues follow the CDC guidelines for prescribing naloxone.

Patients receiving opioids who are at low or average risk of developing opioid use disorders typically have monthly follow-up visits in the Supportive Care Center; those at high risk may be asked to come in more often. On follow-up visits, the staff assesses whether the medicine is controlling the pain and whether the medicine is affecting the patient’s ability to function or causing other adverse effects.

In rare cases, staff members notice signs, such as frequent requests for early refills, suggestive of opioid use disorders. Ms. Edwards and her colleagues developed a system for nurses to identify such warning signs and inform the physicians so that appropriate action can be taken to ensure the patient’s well-being.

Opioid use disorders are multifaceted, and a physician alone may lack the expertise to address all the patient’s needs. To ensure proper care for patients with signs of opioid use disorders, the Supportive Care Center established the compassionate high-alert team (CHAT). A CHAT is a multidisciplinary group whose members vary according to the patient’s needs. In addition to a physician and a nurse, the team typically includes one or more of the following: a psychologist or counselor, who may be needed if the patient is dealing with issues such as anxiety or depression; a social worker, who can help the patient access resources to manage a variety of personal or family issues; a pharmacist, who can answer the patient’s questions

## Interdisciplinary Opioid Crisis Seminar

MD Anderson is hosting a 1-day seminar to educate community health care providers about safe opioid use in the management of cancer-related pain. The Interdisciplinary Opioid Crisis Seminar will be held on April 27, 2018. Topics will include safe opioid prescribing; the impact of state, federal, and global initiatives to curb the opioid crisis; dealing with aberrant opioid-related behavior in cancer survivors; and using urine drug screens and prescription monitoring programs in opioid therapy. Attendees can receive continuing medical education or nursing continuing education credit.

To register online, go to <http://bit.ly/2oVmdFb>.

about medication; and a patient advocate, who makes sure that the patient understands his or her rights and doesn’t feel intimidated.

The team meets quickly to discuss the case and then, together, talks to the patient and discusses appropriate management options. “We provide options in a non-confrontational manner,” Ms. Edwards said.

“The team approach provides a comfortable environment in which the providers and patient can agree on a plan to move forward,” said Suresh Reddy, M.D., a professor in the Department of Palliative, Rehabilitation, and Integrative Medicine, who first developed the CHAT program together with Ms. Edwards. He added that the comfortable environment not only puts patients at ease but also helps avoid burnout issues for staff members.

A group led by Dr. Reddy documented improvements in a cohort of patients after the CHAT program was

implemented. These findings were published in 2017 in *The Oncologist*.

## Sharing lessons learned

“Our approach to opioid management has worked well for us, and we’ve shared the lessons we’ve learned by conducting presentations for other departments at MD Anderson and other institutions,” Ms. Edwards said. She added that MD Anderson will host a seminar on the effect of the opioid crisis on the management of cancer-related pain for community health care providers on April 27, 2018 (see “Interdisciplinary Opioid Crisis Seminar,” this page).

“Physicians need to be informed about prescribing opioids because the landscape is changing,” Dr. Arthur said. “There is increasing state and federal regulatory scrutiny of opioid prescribing. It is now more important than ever for physicians to be cautious when prescribing opioids to their patients, including cancer patients.” ■

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# Hepatitis C Virus Linked to Head and Neck Cancers

Association of HCV with extrahepatic cancers has implications for HCV testing, treatment

By Bryan Tutt

**H**epatitis C virus (HCV), which has long been associated with primary liver cancer and non-Hodgkin lymphoma, has been linked less conclusively to several other cancers, including those of the head and neck. When researchers at The University of Texas MD Anderson Cancer Center noticed a high rate of HCV infection in their head and neck cancer patients, the researchers launched several studies to explore the relationship between HCV and head and neck cancers. Their findings could change standard practices for HCV screening and treatment in patients with cancers of any type.

HCV as a comorbidity in cancer patients has long been a concern at MD Anderson. The institution was among the first cancer hospitals in the world to establish a clinic for HCV treatment, in 2009, and to implement HCV screening for all new patients, in 2016. As a result, MD Anderson has acquired a wealth of data on patients with cancer and HCV.

“When we started to see that, compared with some other cancers, a higher proportion of patients with head and neck cancers tested positive for HCV, we wanted to find out why,” said Harry Torres, M.D., an associate professor in the Department of Infectious Diseases, Infection Control, and Employee Health and the director of the HCV clinic. So far, Dr. Torres and colleagues have found that HCV is associated with head and neck cancers.

“It’s a new, exciting area of research,” Dr. Torres said. “I believe our ongoing studies will find additional important and clinically significant information.”

## HCV and cancer development and outcomes

Dr. Torres and colleagues including Erich Sturgis, M.D., M.P.H., a professor in the Department of Head and Neck

Surgery, conducted a retrospective study of 409 patients with head and neck cancers who were tested for HCV between 2004 and 2014. Analyzed as controls were 694 patients with other tobacco-related cancers—specifically those of the lung, esophagus, or bladder—who were tested for HCV during the same period.

The researchers found that both oropharyngeal and nonoropharyngeal head and neck cancers were associated with HCV seropositivity. Because human papillomavirus (HPV) infection is a factor in the pathogenesis of oropharyngeal cancer, the researchers conducted a subgroup analysis of HCV and HPV status in patients with oropharyngeal cancer. HCV seropositivity was associated with HPV-positive but not HPV-negative oropharyngeal cancers.

“HCV and HPV have common oncogenic pathways,” Dr. Torres said. “Both viruses act on the *TP53* and retinoblastoma tumor suppressor genes. That may explain synergism between the two viruses to cause oropharyngeal cancer.” However, he added, there is much more to be learned about the relationship between the two viruses.

Dr. Torres and colleagues also investigated the effect of HCV infection on survival in patients with oropharyngeal and nonoropharyngeal head and neck cancers. The results of their study of patients with oropharyngeal cancer were recently accepted for publication in *Cancer*, and the researchers plan to have the results of their study of patients with nonoropharyngeal head and neck can-

*Among oropharyngeal cancer patients, Kaplan-Meier analysis shows that patients without the hepatitis C virus (HCV) have a higher progression-free survival rate compared with those who have HCV (P = .001). Adapted with permission from Cancer. 2017. doi: 10.1002/cncr.31146.*

cers ready to present at the 2018 meeting of the American Society of Clinical Oncology (ASCO).

In their study of survival in patients with oropharyngeal cancer, the researchers reviewed the records of patients who were tested for HCV at MD Anderson from 2004 to 2015. The 5-year overall and progression-free survival rates were significantly higher for HCV-negative patients than for HCV-positive patients (see graph above). Furthermore, among HCV-positive patients with oropharyngeal cancer, the 5-year overall and progression-free survival rates were significantly higher for those who underwent antiviral treatment for HCV than for those who did not.

“HCV not only is epidemiologically linked to head and neck cancer but also

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# Understanding Cancer Risk and Risk Factors

## Your risk factors might affect your need for cancer screening

**We often hear that certain foods, such as processed meats, or activities, such as using a tanning bed, can increase a person's risk of getting cancer.** What isn't always clear is how these risks are determined and how substances, behaviors, and personal characteristics come to be thought of as "risk factors."

### Risk factors

Risk factors are the characteristics and behaviors that can increase a person's chances of getting cancer. There are four types of risk factors:

- **Behavioral** (lifestyle) risk factors are behaviors or habits such as smoking, drinking alcohol, not exercising regularly, or not eating healthy foods.
- **Biological** risk factors are physical traits such as race, age, and sex or medical conditions such as precancerous polyps and dense breast tissue.
- **Hereditary** risk factors are specific traits or gene mutations that people inherit from their parents. A person might have a hereditary risk factor if several of his or her family members had the same type of cancer.
- **Environmental/exposure** risk factors are found in our surroundings and include such things as secondhand smoke, pollution, and pesticides. Exposure to viruses such as hepatitis B and C and the human papillomavirus (HPV) or medical treatments such as hormonal therapy and radiation therapy also can increase cancer risk.

### What is risk?

When thinking of cancer specifically, "risk" is the chance of getting cancer for members of a particular group. The two types of risk are

absolute risk and relative risk.

**Absolute risk** is the number of people who will be diagnosed with a type of cancer in a particular time period—for example, in the United States, about 120 of every 1,000 women will be diagnosed with breast cancer in their lifetime. The absolute risk of breast cancer for women in the United States is thus 12%.

**Relative risk** is a comparison of one group's risk of getting a type of cancer to another group's risk. The risk for each group is calculated using data from clinical trials or from agencies like the National Cancer Institute that keep track of cancer statistics. The groups could be assigned according to sex, age, or some other characteristic. A relative risk of 1.0 means the risk of developing cancer is the same for both groups—in other words, the characteristic being studied is not a risk factor for cancer.

A relative risk significantly below 1.0 means people with the characteristic are less likely to get cancer than are those without the characteristic. In contrast, a relative risk significantly above 1.0 means people with the characteristic have a greater risk of getting cancer than do those without the characteristic.

For example, if the relative risk of lung cancer is 20 for a group of smokers compared with a group of nonsmokers, we can conclude that smokers, as a group, are 20 times more likely to get lung cancer than nonsmokers.

If the relative risk of colorectal cancer is 2.3 for a group of people with more than one first-degree relative (parent, brother, sister, or child) who had colorectal cancer compared with

a group whose first-degree relatives did not have colorectal cancer, we can conclude that people in the first group are 2.3 times more likely to get colorectal cancer.

### Risk factors and screening

It's important to remember that these numbers don't reflect any one person's individual risk. Nevertheless, it's important to be aware of any characteristics that might place you at risk of getting cancer.

For example, keep note of your family's cancer history, and keep your doctor informed of any changes in this history. This risk factor may affect your need to be screened for particular types of cancer. Likewise, being aware of behavioral or environmental risk factors, such as smoking or exposure to secondhand smoke, could help you avoid them. And people with certain risk factors may be offered additional screening. ■

### FOR MORE INFORMATION

- Ask your physician
- Visit [www.mdanderson.org](http://www.mdanderson.org)
- To schedule a risk assessment, call MD Anderson's Cancer Prevention Center at 713-745-8040

## Hepatitis C Linked to Head and Neck Cancers

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seems to affect the survival of some of these patients,” Dr. Torres said.

### Implications for physicians

A group of ASCO collaborators, including Dr. Torres and Jessica Hwang, M.D., M.P.H., an associate professor in the Department of General Internal Medicine, are developing an educational statement for oncologists about the importance of HCV in patients with any type of cancer. “First, we are advising physicians to screen cancer patients for HCV,” Dr. Torres said. “Second, we’re urging physicians to refer HCV-positive patients for antiviral therapy.” He added that many cancer patients who are found to have HCV are able to undergo HCV treatment and cancer treatment at the same time.

Treating HCV in patients with non-Hodgkin lymphoma is known to improve oncologic outcomes. In fact, some patients with indolent lymphoma experience a complete remission of their cancer after antiviral treatment for HCV. The benefits of HCV treatment are not as well known in patients with other cancers, but Dr. Torres said that curing the virus will likely have long-term effects beyond the prevention or slowing of cirrhosis.

Treating HCV in cancer patients may also prevent second primary cancers (e.g., primary liver cancer, non-Hodgkin lymphoma) from arising. Dr. Torres has begun researching this topic in collaboration with colleagues including Ernest Hawk, M.D., M.P.H., the vice president of Cancer Prevention and Population Sciences

and executive director of the Duncan Family Institute for Cancer Prevention and Risk Assessment.

“We want to know if we can prevent second primary cancers if we identify and treat HCV early enough,” Dr. Torres said. “And we have some preliminary data to support that HCV-associated second primary cancers are common and lethal in cancer survivors.”

HCV testing and treatment in cancer patients will become even more important if other cancers that have been anecdotally linked to HCV—such as cancers of the digestive tract, thyroid, kidney, prostate, lung, and nonepithelial skin—have their associations with the virus confirmed by studies similar to Dr. Torres’s. He said, “I expect that we’ll add more cancers to the list of malignancies associated with HCV.” ■

### FOR MORE INFORMATION

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### FURTHER READING

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