New cancer drugs discovered at U-M head to clinical trials

One compound targets cell death blockers, other impacts tumor suppressor protein

Researchers at the University of Michigan Comprehensive Cancer Center have developed two new types of drug compounds that show potential in animal and laboratory studies to treat multiple types of cancer. One compound is already being tested in clinical trials and the other has clinical trials in development.

continued on page 2
The first compound, called AT-406, was shown to effectively target proteins that block normal cell death from occurring. Blocking these proteins caused tumor cells to die, while not harming normal cells. The researchers believe the drug could potentially be used alone or in combination with other treatments.

“Removing key apoptosis blockades in tumor cells is a completely new cancer therapeutic approach and could have benefit for the treatment of many types of human tumors,” says study author Shaomeng Wang, Ph.D., the Warner-Lambert/Parke-Davis Professor of Medicine and director of the Cancer Drug Discovery Program at the U-M Comprehensive Cancer Center.

Wang’s laboratory has been pursuing new cancer treatments aimed at the apoptosis pathway since 2003. His team designed and made AT-406 and tested it in the laboratory in 2006. The small-molecule drug hones in on the proteins — called inhibitor of apoptosis proteins or IAPs — that block cell death. The researchers found that AT-406 destroyed these proteins in cancer cells. Meanwhile, the drug had little to no effect on normal cells.

In animal models, the drug shrank tumors but caused few side effects. The drug is designed to be taken by mouth, which researchers say will make it easier than traditional intravenous chemotherapies to administer.

AT-406 is already being tested in clinical studies. After extensive pre-clinical testing, Ascenta Therapeutics began the first clinical trial in 2010 testing AT-406 for cancer treatment. This trial, which is being tested in all solid tumors, is offered at the U-M Comprehensive Cancer Center, Duke University and the Mayo Clinic. Ascenta has also recently opened a second trial of AT-406 in high-risk acute myeloid leukemia at the U-M Comprehensive Cancer Center. Several more clinical trials are planned.

“Our research goal and our passion is to translate our science and discovery into new and effective medicines for patients,” Wang says. “I am delighted to see the drug we have designed, made and tested in our laboratory now being given to patients right here in the same building.”

The second type of drug compound developed at U-M is designed to activate the tumor suppressor p53 protein. P53 is inactivated in a significant number of human cancers. In some cases, it is because another protein, MDM2, binds to p53 and blocks its tumor suppressor function.

“For the first time, we showed that activation of p53 by our highly potent and optimized MDM2 inhibitors can achieve complete tumor regression in a mouse model of human cancer.”

— Shaomeng Wang, Ph.D.

This allows the tumor to grow unchecked. Researchers tested two new compounds and found they blocked MDM2 from binding to p53, consequently activating p53.

“For the first time, we showed that activation of p53 by our highly potent and optimized MDM2 inhibitors can achieve complete tumor regression in a mouse model of human cancer,” says Wang, whose team also developed these compounds.
Many traditional cancer drugs activate p53 but they do so by causing DNA damage in both tumor cells and normal cells, causing side effects. These new MDM2 inhibitors activate p53 while avoiding the DNA damage common with other drugs. In this study, which was done in collaboration with Ascenta Therapeutics and Sanofi-Aventis, researchers showed that these new drugs shrank tumors without significant side effects.

Because p53 is involved in all types of human cancer, the new drug has potential to be used in multiple types of cancer. Further, the researchers also identified certain markers in tumors that predict which ones will be particularly sensitive to the MDM2 inhibitor, which would allow physicians to target the drug only to patients most likely to benefit.

U-M researchers are working with Ascenta and Sanofi-Aventis to further test these compounds and develop clinical trials.

Disclosure: Patent applications covering AT-406 are exclusively licensed to Ascenta Therapeutics, a privately-held, clinical stage biopharmaceutical company co-founded by Wang. The MDM2 inhibitors have been licensed to Ascenta Therapeutics, then sublicensed to Sanofi-Aventis for clinical development, and the University of Michigan receives milestone payments and royalties. Wang owns stocks and stock options in Ascenta and serves as a consultant for Ascenta.

FOR MORE INFORMATION


News Archive: www.uofmhealth.org/News/cancer_drug_0329

U-M study: Parents trust physicians most on information about vaccine safety

Most parents get their information about vaccines from their children’s physicians, but some also consider public health officials, other parents, friends and family members and even celebrities as sources of vaccine information.

These are the results of a national survey conducted by University of Michigan researchers to determine how much parents trust different sources of information in regards to vaccination.

The results of this study were published this past April in the journal Pediatrics.

“Parents get information about children’s vaccines from many sources,” says Gary L. Freed, M.D., M.P.H., chief of the Division of General Pediatrics and director of the Child Health Evaluation and Research (CHEAR) Unit. “The source parents trusted most is their children’s doctor.”

Researchers surveyed 1,552 parents of children ages 17 years and younger on topics including parental trust of sources of information about vaccines.

A majority of parents reported trusting their child’s doctor ‘a lot’ (76%). Other sources trusted ‘a lot’ by parents were other health care providers (26%) and government vaccine experts/officials (23%). Trust also varied by race/ethnicity: white and Hispanic parents were more likely than black parents to trust family and friends ‘a lot’ or ‘some,’ and Hispanic parents were more likely than white or black parents to trust celebrities ‘a lot’ or ‘some’ for vaccine-safety information.

“Those who design public health efforts to provide evidence-based information must recognize that different strategies may be required to reach all groups of parents,” says Freed.

The research was conducted as part of the C.S. Mott Children’s Hospital National Poll on Children’s Health. In addition to Freed, other authors include Sarah J. Clark, M.P.H., Amy T. Butchart, M.P.H., Dianne C. Singer, M.P.H, and Matthew M. Davis, M.D., M.A.P.P., of the University of Michigan

FOR MORE INFORMATION

Citation: “Sources and Perceived Credibility of Vaccine-Safety Information for Parents,” Pediatrics. doi: 10.1542/peds.2010-1722P

Gary L. Freed, M.D., M.P.H., chief of the Division of General Pediatrics and director of the Child Health Evaluation and Research (CHEAR) Unit

“Parents get information about children’s vaccines from many sources. The source parents trusted most is their children’s doctor.”

— Gary L. Freed, M.D., M.P.H.
Lorraine Poppleton saw 24 doctors in the course of a year, but they were dismissive of her bouts of dizziness, tinnitus and the intrusion of an occasional whistling and tapping sound like Morse code.

“They told me I was crazy, that it was just in my head,” says Poppleton, a legal secretary at an international law firm in midtown Manhattan. “I couldn’t walk straight. I would veer to the right and was unsteady when standing and dizzy when sitting. Then one day, I was getting up and it felt like someone who weighed a ton flattened me back into the bed.”

She credits New York neurologist Joseph C. Casarona, M.D., for being the first doctor to take her condition seriously. He prescribed Antivert (meclizine) for her vertigo, but it only gave her relief for two days. Casarona then ordered an MRI which revealed Poppleton had a tumor growing on her auditory nerve — an acoustic neuroma.

Poppleton’s case is a classic example of a patient whose quality of life would have been unnecessarily damaged by the predominant surgical approach to removing these tumors, says Steven A. Telian, M.D., the John L. Kemink Professor of Neurotology in the Department of Otolaryngology at the University of Michigan Medical School.

“Doctors can let their patients know that there are options out there that can preserve hearing in a large percentage of acoustic neuroma cases,” Telian says.

Poppleton’s tumor remained stable for about a year and a half, but a follow-up scan in 2009 showed it was growing.
“They told me, ‘It’s on the move,’ ” Poppleton recalls.

She sought out three opinions from doctors at major New York medical centers. They all recommended removing the tumor using a translabyrinthine approach, which enters the auditory nerve canal through the mastoid bone behind the ear. The technique always results in a complete loss of hearing.

“They all told me the same thing,” she says. “I’d lose my hearing. I could expect facial paralysis. My life would never be the same. I was told by one very prominent doctor that if his colleague who had undergone this surgery could live with the side effects, so could I.”

Poppleton thought she had no choice. The young, active grandmother either had to undergo surgery that she was told might put her into a wheelchair for the rest of her life or risk the tumor spreading to her brain.

Two weeks before her scheduled surgery, however, her son-in-law, a house officer in U-M’s Department of Dermatology, informed her of an interdisciplinary program at U-M skilled in newer techniques. The team offers an innovative approach that studies have shown has an 80 percent success rate for preserving hearing.

The middle fossa microsurgical technique, as it is called, approaches the tumor from above the ear.

“It gives us our best opportunity for hearing preservation, but a lot of major centers don’t even consider it strongly,” says B. Gregory Thompson Jr., M.D., professor of neurosurgery at the U-M Medical School. “It requires a high degree of technical expertise.”

Doctors at U-M have refined this technique over time, innovating the use of a wider opening that gives the surgeon more room and a better angle from which to attack the tumor, and employing sharper dissection tools, Thompson explains.

“It’s a little counterintuitive, but we’ve learned from our work on brain aneurysms that using sharper tools under high magnification, there’s less likely to be a rupture because there’s less of the tugging you get with blunt dissection,” he says. “The same principle applies to preserving the auditory and facial nerves.”

Not long after forwarding her records for review, Poppleton flew to Michigan, where she had a series of preoperative tests on a Thursday and Friday. On Monday she had surgery.

She was released less than a week after the successful operation by Telian and Thompson. She was able to hear normally and soon was back at work full time, and back to jogging, playing tennis, dancing and trying to keep up with her five grandchildren.

“The take-away message is that before a patient undergoes any procedure that will sacrifice hearing, their doctors need to assess if they are a candidate for one of the approaches that can preserve hearing — either middle fossa or posterior fossa,” says Telian.

Not all centers that perform hearing preservation techniques are equally successful, Thompson cautions. Patients should inquire about prospective centers’ experience and hearing preservation rates.

ACOUSTIC NEUROMA

Each year 2,000 to 3,000 people in the U.S. are diagnosed with an acoustic neuroma. Three out of every five patients are female.

U-M CRANIAL BASE PROGRAM

In U-M’s Cranial Base program, specialists in Otolaryngology, Neurosurgery, Ophthalmology, Radiation Oncology and Medical Oncology work together to ensure comprehensive, appropriate treatment and the highest quality outcomes possible.

FOR MORE INFORMATION

Cranial/Skull Base Tumors: www.med.umich.edu/cranialbase/
While it’s generally known that African Americans have the highest risk for glaucoma, a new study reports that Asian Americans face a significantly increased risk of developing glaucoma, a potentially blinding disease.

Joshua D. Stein, M.D., M.S., a glaucoma specialist at the U-M Kellogg Eye Center, reviewed claims data of more than 44,000 Asian Americans over age 40 who were enrolled in a nationwide managed care network. He found Asian Americans’ risk for open-angle glaucoma to be 51% higher than that of non-Hispanic whites.

Glaucoma is a condition that affects the optic nerve, the structure responsible for transmitting visual information from the eye to the brain so it can be processed and interpreted. Damage to the optic nerve results in progressive loss of peripheral vision and, if left untreated, can lead to irreversible blindness.

Glaucoma is the second most common cause of blindness worldwide and, in the United States, over two million people and almost two percent of all adults over age 40 have glaucoma.

The study, published in June in *Ophthalmology,* has implications for eye doctors, says Stein, who notes that Asian Americans are the second fastest growing population in the U.S. “Clinicians should be aware that their Asian American patients are at increased risk for glaucoma and should monitor them for signs of the disease,” he says.

Stein explains, “Most forms of glaucoma are asymptomatic early in the course of the disease. Individuals who have risk factors for glaucoma — older age, nonwhite race, and a family history of glaucoma — should have routine eye exams for the disease. This exam includes checking intraocular pressure, examining the optic nerve and, when appropriate, performing visual field testing to detect loss of peripheral vision, a key sign of glaucoma.”

The study detailed the Asian American ethnic groups most likely to develop the three main types of glaucoma: open-angle glaucoma (OAG, the most common form), narrow-angle glaucoma (NAG), and normal-tension glaucoma (NTG).

The rate of NAG was higher in Asian Americans than in any other racial group in the study and highest of all among Chinese and Vietnamese Americans. With NAG, the part of the eye that drains excess fluid becomes blocked and pressure builds up. The patient usually feels severe, rapid-onset pain and needs immediate treatment to prevent vision loss.

The rate of NTG was 3 to 10 times higher in Japanese Americans than other Asian ethnicities and nearly all of the Asian subgroups were at higher risk than non-Asian Americans. With NTG, the optic nerve sustains damage even though eye pressure remains within “normal” levels.

Eye doctors should look for signs of glaucoma when evaluating Asian American patients over age 40. “For example, the inner eye angle anatomy of patients of Chinese or Vietnamese ancestry should be carefully examined,” Stein says. “And since NTG won’t be detected by simply measuring intraocular pressure, eye doctors need to assess the optic nerve and, when appropriate, perform visual field testing in patients whose ethnicity makes them more susceptible to this type of glaucoma,” he adds.

**FOR MORE INFORMATION**

Reference: Volume 118, Issue 6, Pages 1031-1037, June 2011

Glucoma, Cataract, and Anterior Segment Disease: [www.kellogg.umich.edu/patientcare/glaucoma.service.html](http://www.kellogg.umich.edu/patientcare/glaucoma.service.html)

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**The inner eye angle anatomy of patients of Chinese or Vietnamese ancestry should be carefully examined.**

— Joshua D. Stein, M.D.

Increased cupping of the optic nerve and thinning of the neuroretinal rim tissue are characteristic features of open-angle glaucoma.
Eye symptoms may signal bigger problems for cancer patients

Eye problems in patients with cancer should send up a red flag, says Hakan Demirci, M.D., director of the Kellogg Eye Center’s new Orbital and Ocular Oncology Service. These eye symptoms may reveal the presence of an ocular tumor, which may be an early sign of systemic metastasis.

Demirci is developing a multidisciplinary network of physicians at the Eye Center and throughout the U-M Health System to manage care of patients with ocular cancers. “Our goal is to communicate with colleagues and patients about symptoms that can have profound implications for the patient’s health,” he says.

The most common intraocular tumor is often the result of metastasis from primary cancer of the breast or lung, observes Demirci. He cites studies showing that 47 percent of intraocular metastatic tumors arise from breast cancer, while 20 percent of ocular metastasis can be secondary to lung cancer.

Yet the symptoms are not always obvious. About two-thirds of these patients will complain of blurry vision, while the rest may have no symptoms. Upon clinical examination, metastatic cancers are likely to be yellow in color, plateau shaped, and associated with subretinal fluid; frequently, the tumor is located on the macula or between the macula and equator.

“When eye symptoms arise in a cancer patient, it is critical that an ophthalmologist become involved in that patient’s care,” says Demirci. Recent studies show that when cancer metastasizes to the eye, the risk of it spreading to the brain or central nervous system increases significantly. Imaging of the brain and central nervous system should be part of systemic evaluation.

If detected early, metastatic lesions can be successfully treated with modalities that include external beam radiotherapy or radioactive plaque brachytherapy, systemic and hormone therapies, and, in selected cases, an emerging class of immunotherapies. “There is always concern that ocular tumors go undetected in patients with advanced cancers,” says Demirci. “In the face of multiple health problems, these patients may not mention eye complaints.”

Other concerns arise when the eye is the primary site of a tumor, as in uveal melanoma, the most common primary eye tumor. While diagnosis may be challenging due to atypical clinical presentation, early detection of uveal melanoma is important.

Demirci believes that advances in ophthalmic genetics and emerging treatments will improve systemic outcomes for patients with ocular tumors. “With new gene profiling tests, we are better able to identify the uveal melanoma patients who carry a higher risk of developing systemic metastasis,” he notes.

Kellogg ophthalmologists are also working closely with colleagues in radiation oncology to adopt new techniques to minimize side effects associated with radioactive plaque brachytherapy. And clinical trials are now available at the U-M Comprehensive Cancer Center to evaluate new treatments for patients with systemic metastasis from uveal melanoma.

Demirci’s hope is that all physicians become more vigilant in looking for eye disease in cancer patients. “With early diagnosis and treatment, these patients can expect to have improved vision and better quality of life,” he says.

FOR MORE INFORMATION

Orbital and Ocular Oncology: www.kellogg.umich.edu/eyecancer
Weight returning after bariatric surgery is a reality for many patients. And research has shown that patients who continue specialty care after bariatric surgery with physicians who have expertise in obesity medicine and or dieticians do better in the long run, with more successful weight loss.

One challenge is managing patients’ metabolic conditions. “At least 50 percent of patients seeking bariatric surgery are diabetic and bariatric surgery is now being looked at as an intervention to treat and cure diabetes,” says Elif Oral, M.D., assistant professor of internal medicine in the Division of Metabolism, Endocrinology and Diabetes at U-M. “In the future, endocrine specialists will probably have more of a role in referring patients to bariatric surgery and also to follow and guide diabetes related care and surveillance for complications in the years to come. As a corollary, bariatric surgeons are getting more and more involved in the treatment of diabetes.”

Another concern with these patients is prevention and management of metabolic complications. For example, some types of surgery lead to vitamin D and calcium deficiency.

“It may take as much as 12 to 18 months for complications to set in, especially if the patients neglect to take their supplements,” says Oral. “Occasionally, problems with hypoglycemia are seen too.”

To help these patients, whether or not they had their bariatric surgery at U-M, the U-M Health System has launched a new Post-Bariatric Surgery Clinic to help with ongoing care for patients after follow-up with their surgeon has ended. The clinic opened in fall 2010 and is located in Domino’s Farms, Lobby C in the Metabolism, Endocrinology and Diabetes Clinic site.

Oral, who is medical director of the U-M Bariatric Surgery Program, is the clinic’s director. Andrew Kraftson, M.D., clinical instructor in internal medicine, and Angela Subauste, M.D., assistant professor of internal medicine, are co-directors. The dietitians are Catherine Kraus and Amy Lockwood.

U-M performs three types of bariatric surgery: laparoscopic gastric bypass, adjustable band, and sleeve gastroectomy. The U-M Bariatric Surgical team also runs a collaborative of all bariatric surgery programs throughout the state of Michigan. Patients who come through any bariatric surgery program in Michigan can be referred to the Post-Bariatric Surgery Clinic for follow-up care.

FOR MORE INFORMATION
Metabolism, Endocrinology & Diabetes (MEND): www.med.umich.edu/intmed/endocrinology/index.htm
Aortic stenosis: Interventional vs. surgical approach being compared in new trial

A national clinical trial to offer patients a less invasive approach to replacing diseased aortic valves has begun, and is now recruiting up to 1,200 patients at 40 sites including the University of Michigan Cardiovascular Center, a leader in heart valve replacement.

The study, called the Medtronic CoreValve U.S. Pivotal trial, will examine an investigational alternative to open heart surgery for patients with severe aortic stenosis.

About 100,000 Americans are diagnosed with severe aortic stenosis each year, but one-third of patients, due to age or frail health, are considered too high-risk for traditional surgery.

“Through this trial we are investigating a minimally invasive procedure for the thousands of patients diagnosed each year with severe aortic stenosis,” says U-M cardiac surgeon G. Michael Deeb, the Herbert Sloan Collegiate professor of surgery. “There is a tremendous unmet need for a safe and effective treatment that will help them live longer and feel better.”

It’s not uncommon for patients to experience chest pain, dizziness, shortness of breath, feel faint with activity, and suffer heart palpitations. As the population ages, more Americans will be susceptible to aortic stenosis, he says.

Severe aortic stenosis is often unpreventable and may be related to age, buildup of calcium deposits causing narrowing, radiation therapy, medications, history of rheumatic fever or high cholesterol.

The U-M study team is led by Stanley J. Chetcuti, M.D., associate professor of internal medicine, Paul Michael Grossman, M.D., associate professor of internal medicine, Deeb, and Himanshu J. Patel, M.D., associate professor of surgery.

All are part of the U-M aortic program that performs over 500 surgical valve procedures a year — more than any other Michigan program.

In the CoreValve trial, surgeons and interventional cardiologists work together to perform the procedure called transcatheter aortic valve implantation. It allows access to the diseased aortic valve percutaneously, usually an artery in the leg, rather than through open surgery.

“There can be many advantages to that,” says Grossman, study co-principal investigator and director of the cardiac catheterization laboratory at the Veterans Administration Ann Arbor Healthcare System. “Open surgical procedures are often associated with long recovery times and there are many patients who are too sick to tolerate and recover from major surgery.”

Dr. Chetcuti, the study co-principal investigator, director of the cardiac catheterization laboratory at the Cardiovascular Center and the Eric J. Topol professor of cardiovascular medicine, says: “The critical part of the study is to make sure it is done well and that we answer the questions: Is this technology safe and does it make a difference to our patients.”

The trial adds to the U-M Cardiovascular Center’s tradition of research expertise. In the past five years alone, its physicians and scientists have participated in more than 700 cardiovascular clinical trials.

FOR MORE INFORMATION

Heart & Vascular Care: www.uofmhealth.org/corevalve

Open surgical procedures are often associated with long recovery times and there are many patients who are too sick to tolerate and recover from major surgery.”

— Paul Michael Grossman, M.D.
New tool aims to improve measurement of primary care depression outcomes

Positive measures can aid physicians in evaluating treatment success, U-M study says

Primary care doctors have long been on the front lines of depression treatment. Depression is listed as a diagnosis for 1 in 10 office visits and primary care doctors prescribe more than half of all antidepressants.

Now, physicians at the University of Michigan Health System have developed a new tool that may help family physicians better evaluate the extent to which a patient’s depression has improved.

The issue, the researchers explain, is that the official definition of when a patient’s symptoms are in remission doesn’t always match up with what doctors see in a real-world practice, especially for patients with mild to moderate symptoms.

“There was a disconnect between the measurements and what people were feeling, so we knew we didn’t have the whole picture,” says study author Michael Klinkman, M.D., M.S., professor of family medicine at the U-M Medical School.

The study was published in the May/June issue of General Hospital Psychiatry.

“Rather than simply going down a list and checking off a patient’s lack of individual symptoms, we believe there are also positive signs that are important — a patient’s feeling that they are returning to ‘normal,’ their sense of well-being, their satisfaction with life and their ability to cope with life’s ups and downs,” says lead author Donald E. Nease Jr., M.D., adjunct professor of family medicine at U-M.

The researchers developed a series of five questions — such as, “Over the last two weeks, did you feel in control of your emotions?” — that they hope will help doctors better understand a patient’s inner landscape.

The remission criteria spelled out in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) doesn’t necessarily correspond to a patient’s own sense of recovery, says Klinkman, also a member of the U-M Depression Center.

For example, a patient could meet all the criteria for full remission, but still not feel that he had recovered. The U-M questionnaire, which is called Remission Evaluation and Mood Inventory Tool, or REMIT, is intended to add the patient’s subjective sense of recovery into the equation.

Rather than a replacement for current tools and measurements, REMIT is intended to complement them. But unlike other tools that require a company’s permission to use, the REMIT tool is available without charge to any physician or other provider who wants to use it.

The researchers used the REMIT tool alongside the Patient Health Questionnaire (PHQ), the current “gold standard” for monitoring people with depression.

The data showed that by adding in the REMIT questions, about one-third of patients with mild depression were not in remission, as their PHQ score would indicate. Additionally, about one-third of moderately depressed patients were doing better than their PHQ scores alone would denote.

“Using just the PHQ score across our study population, we saw about 60 percent accuracy in reflecting a patient’s remission compared to the patient’s sense of his or her own recovery,” says Nease, who was an associate professor at the time of the research. “If you add in the REMIT questions, we get above 70 percent. This can give doctors new insights when making treatment choices, such as changing a patient’s medication or dosage.”

“There was a disconnect between the measurements and what people were feeling, so we knew we didn’t have the whole picture.” — Michael Klinkman, M.D., M.S.
The tool has already proven valuable in clinical practice,” Klinkman says. “There are patients whose recovery looks good on the PHQ, but who are still experiencing trouble with everyday life and who aren’t feeling quite back to normal. There are others whose PHQ scores say they’re not in remission and that we should treat them more aggressively — but they feel like they’ve bounced back completely, they’re happy again. In those situations, if the treatment has been good enough for them, it could also be good enough for us.”

The current research looked at a single snapshot in time for nearly 1,000 patients. The next step will be to track patients over time and refine scoring using longitudinal data.

In addition to Nease and Klinkman, the study’s authors include James E. Aikens, Ph.D. and Ananda Sen, Ph.D. of U-M, and Kurt Kroenke, M.D., of Roudebush VA Medical Center and Indiana University.

The research was partially supported by a grant from Eli Lilly & Co., which did not have editorial control over the content of the article. The Regents of the University of Michigan placed the tool into the public domain.

For more information


REMIT — REMISSION EVALUATION AND MOOD INVENTORY TOOL

For each question, please circle the number that corresponds to your answer.

<table>
<thead>
<tr>
<th>Over the last 2 weeks…</th>
<th>None of the time</th>
<th>A little of the time</th>
<th>Some of the time</th>
<th>Most of the time</th>
<th>All of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Did you feel happy?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2. Did you feel content?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3. Did you feel in control of your emotions?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4. Did you bounce back when things went wrong?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5. Did the future seem dark to you?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

While further research is ongoing to develop a scoring system for REMIT, the authors note that the lower the score out of 20, the closer a patient is approaching full recovery. Doctors interested in using REMIT before that research is complete should take into account responses on individual REMIT questions, how low the absolute total score is and whether it is improving over time. These can serve as indications that a patient is recovering.

“The tool has already proven valuable in clinical practice,” Klinkman says. “There are patients whose recovery looks good on the PHQ, but who are still experiencing trouble with everyday life and who aren’t feeling quite back to normal. There are others whose PHQ scores say they’re not in remission and that we should treat them more aggressively — but they feel like they’ve bounced back completely, they’re happy again. In those situations, if the treatment has been good enough for them, it could also be good enough for us.”

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