CORPORATE NEWS

MASSIVEBIO

YEAR:2023 / ISSUE:04

"AN INTERVIEW WITH **MASSIVE BIO CO-FOUNDER CAGATAY CULCUOGLU**"

UPDATE ON **ESOPHAGEAL CANCER**

KEEPING A COOLER HEAD

CAN AN APP CURE **LONELINESS?**

ARE YOU GETTING **THE BEST TREATMENT?**

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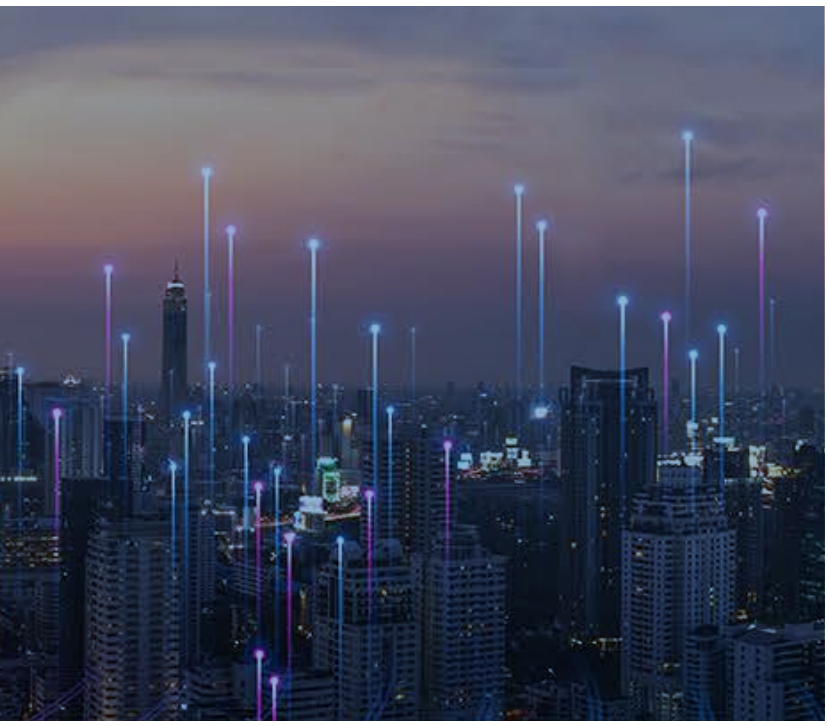

MASTHEAD

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MASSIVEBIO

A MESSAGE FROM SELIN

Spring, as poets like to remind us, is a time of new beginnings. While Massive Bio began as a company that uses artificial intelligence (AI) to match cancer patients to clinical trials, we're always innovating and plan to introduce a new product this year: an AI-powered drug-matching platform that will allow oncologists to identify more cancer treatment options for their patients, including recently approved drugs, as well as agents being evaluated in current clinical trials. Our new drug-matching platform will also help biotech and pharmaceutical companies operate more efficiently by improving their ability to target which patients and physicians need the latest drugs.

To be sure, patient recruitment is just part of what we do at Massive Bio, and this new offering builds on our long-term vision—what I think of as the Amazon-ization of the patient journey. Our ultimate goal is to empower patients to use data and technology in order to get the maximum benefit from the healthcare system in the comfort of their own homes, anywhere in the world and regardless of their financial circumstances, until the time comes when it's absolutely necessary to visit a healthcare facility.

We plan to roll out more offerings designed to assist patients with clinical decision making and offer support as they travel the "last mile" to getting the treatment that's right for them. At Massive Bio, our goal is to bring new beginnings to patients' lives every day of the year.

Selin Kurnaz
PhD, Co-founder and CEO

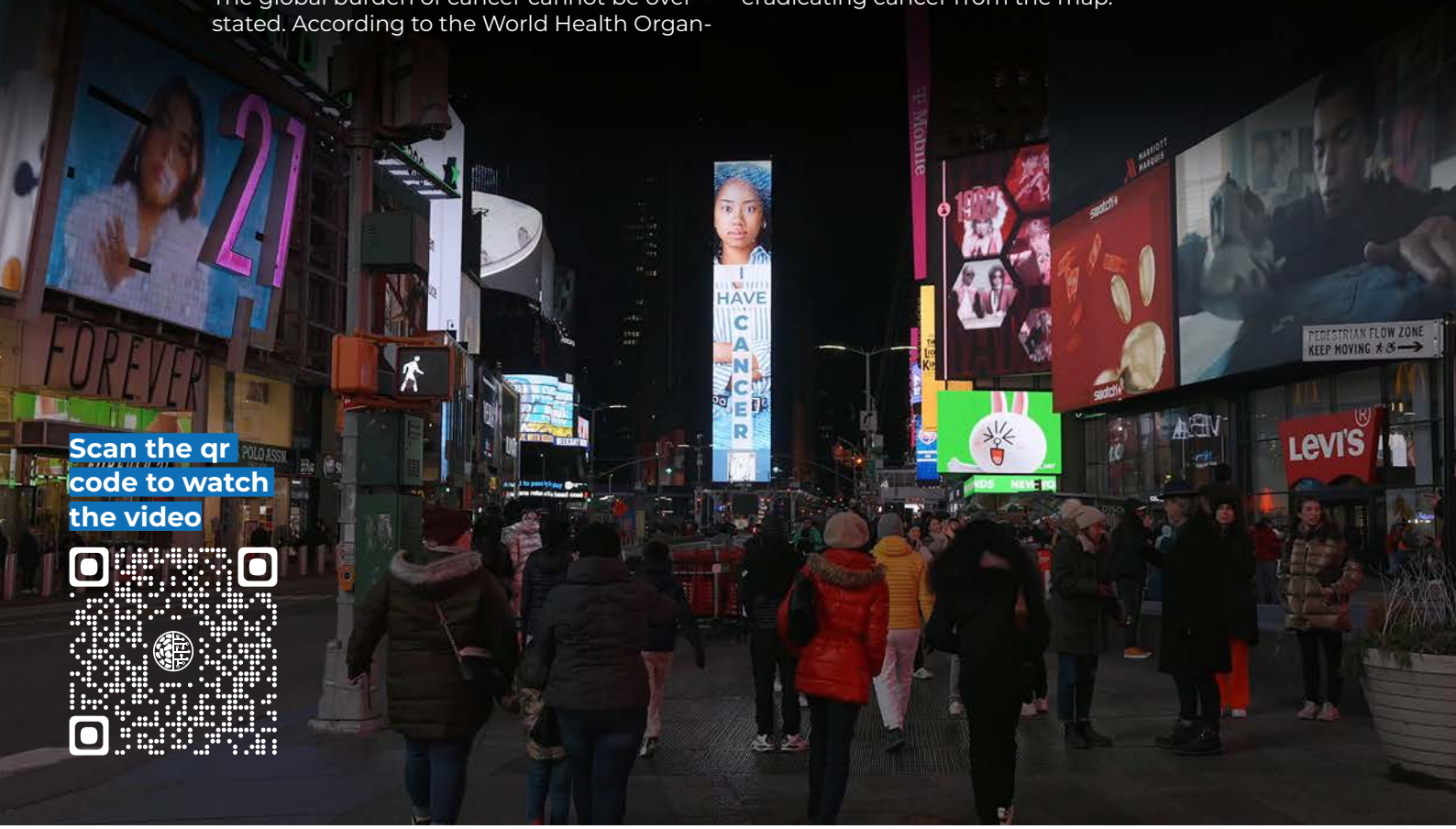
Massive Bio News Briefs

Massive Bio Participated in World Cancer Day Events in Times Square
To honor World Cancer Day, Massive Bio created a video to raise awareness about cancer and the potential for artificial intelligence to help patients find innovative new treatments, which was displayed in New York City's famed Times Square on February 4, 2023.

World Cancer Day is held every year on February 4 and was established in 2000 by the Union for International Cancer Control (UICC), which is the largest and oldest organization devoted to reducing the burden of cancer, promoting equity in cancer care, and making cancer control a priority for governments around the world.

The global burden of cancer cannot be overstated. According to the World Health Organization, approximately 10 million people die of cancer each year. Approximately 70 percent of cancer deaths occur in low- and middle-income countries. Yet, experts estimate that at least one-third of cancer deaths can be prevented with routine screening, early diagnosis, and access to effective treatments.

Massive Bio has conducted several global campaigns to increase awareness of the benefits of preventive measures and access to treatments. Massive Bio's current "I Have Cancer" social media campaign was launched last November and has reached millions of people around the world. The new video that Massive Bio displayed in Times Square on World Cancer Day is yet another expression of the company's commitment to improving the lives of oncology patients and eradicating cancer from the map.



Scan the qr code to watch the video

MASSIVE BIO is named to the New York City Digital Health 100

Massive Bio Launched an Aid Campaign for Earthquake Relief in Turkey

A magnitude 7.8 earthquake shook Turkey and Syria on February 6, 2023, with major tremors continuing in the following days. The death toll from this disaster eventually surpassed 50,000 people and thousands of buildings were destroyed. In response, Massive Bio launched an aid campaign to contribute to the relief effort that delivered urgently needed supplies to the earthquake-affected areas. In addition to making a contribution toward this cause as a company, Massive Bio also offered individual donations on behalf of each of its employees.

Massive Bio Was Named to NYC Digital Health 100 for the Second Time

Massive Bio was honored to be named to the New York Digital Health 100 (DH100) for the second consecutive year. The DH100, which is published annually by Digital Health New York (DHNY), showcases the most exciting and innovative health start-ups in the New York region and is featured in the New York Healthcare Innovation Report 2023. The report is an in-depth look at the leaders, trends, and data that are shaping healthcare innovation in New York. DHNY's stated goal is to "create a connected community that shares ideas, leads in new directions, and builds success for the entire healthcare ecosystem."

Competition for inclusion in this year's DH100 was intense, as DHNY received twice as many applications compared to 2022. Massive Bio was named one of the top 10 companies in the Data & Platform: Analytics & Insights category. "Massive Bio has been headquartered in New York City since it was founded in 2015, so being selected is very important to us," said Selin Kurnaz, co-founder and CEO of Massive Bio. "Although the health ecosystem includes very complex and challenging processes worldwide, our adventure that started in New York City has spread to 12 countries in a short time and reached more than 100,000 cancer patients."

Massive Bio will continue to innovate and develop its artificial intelligence capabilities, added Arturo Loaiza-Bonilla, MD, co-founder and chief medical officer of Massive Bio. "We envision a world where patients are no longer burdened with navigating the clinical research field and can focus on what matters, such as their health and well-being," said Loaiza-Bonilla. "At the heart of our mission is the belief that every cancer patient deserves the opportunity to explore all possible treatment options, and our platform is committed to making that a reality."

Selin was a Panelist at the SCOPE Summit

Massive Bio CEO Selin Kurnaz was a panelist at the SCOPE Summit, one of the important events in the field of clinical research, which took place on February 6-9, 2023, in Orlando, Florida. The annual summit is a gathering of leaders in clinical operations and research to discuss and share ideas about critical issues facing the industry, which this year included

DIGITAL EVENT

March 28th at 02:00 pm ET

HOW IS AI DRIVING PERSONALIZED CANCER TREATMENT?

Selin Kurnaz, Ph.D.
CEO of Massive Bio

Cagatay Culcuoglu
CTO of Massive Bio

Oz Huner
CPO of Massive Bio

Moderator:
Arturo Loaiza-Bonilla, MD
Chief Medical Officer of Massive Bio

addressing racial inequalities in clinical trials, conducting clinical trials in the face of global crises (including the COVID-19 pandemic, war, hyperinflation, and supply chain disruptions), using next-generation data sources, and many others. "SCOPE brings together those driving innovation in digital health," said Kurnaz. "As Massive Bio, we were excited to meet our current and new customers and business partners."

Massive Bio Launches New Webinar Series

On March 28, Massive Bio launched a new webinar series with a roundtable discussion titled "How is AI Driving Personalized Cancer Treatment?" These webinars, which are free and available for viewing on the Massive Bio Facebook page, will be moderated by Arturo Loaiza-Bonilla, MD, chief medical officer and co-founder of Massive Bio. Panelists at the premier webinar included:

- Selin Kurnaz, Ph.D. chief executive officer and co-founder of Massive Bio
- Çağatay Çulcuoğlu, chief technology officer, chief operating officer, and co-founder of Massive Bio
- Oz Huner, chief product officer at Massive Bio

During this event, participants discussed how AI is revolutionizing the delivery of healthcare—with a focus on cancer care and management—by individualizing treatment regimens to achieve better outcomes. Kurnaz and her Massive Bio colleagues explained how the company uses AI to rapidly and accurately identity clinical trials of innovative new oncology therapies for cancer patients, and described new AI-based products the company is rolling out that will further improve cancer treatment. Future webinars hosted by Massive Bio will examine how clinical trials can benefit patients with hematologic cancers and the role of cancer biomarkers in oncology clinical trials and therapies.

MASSIVE BIO AND NEOGENOMICS **Announce Collaboration to Accelerate Oncology Drug Discovery and Improve Patient Care**

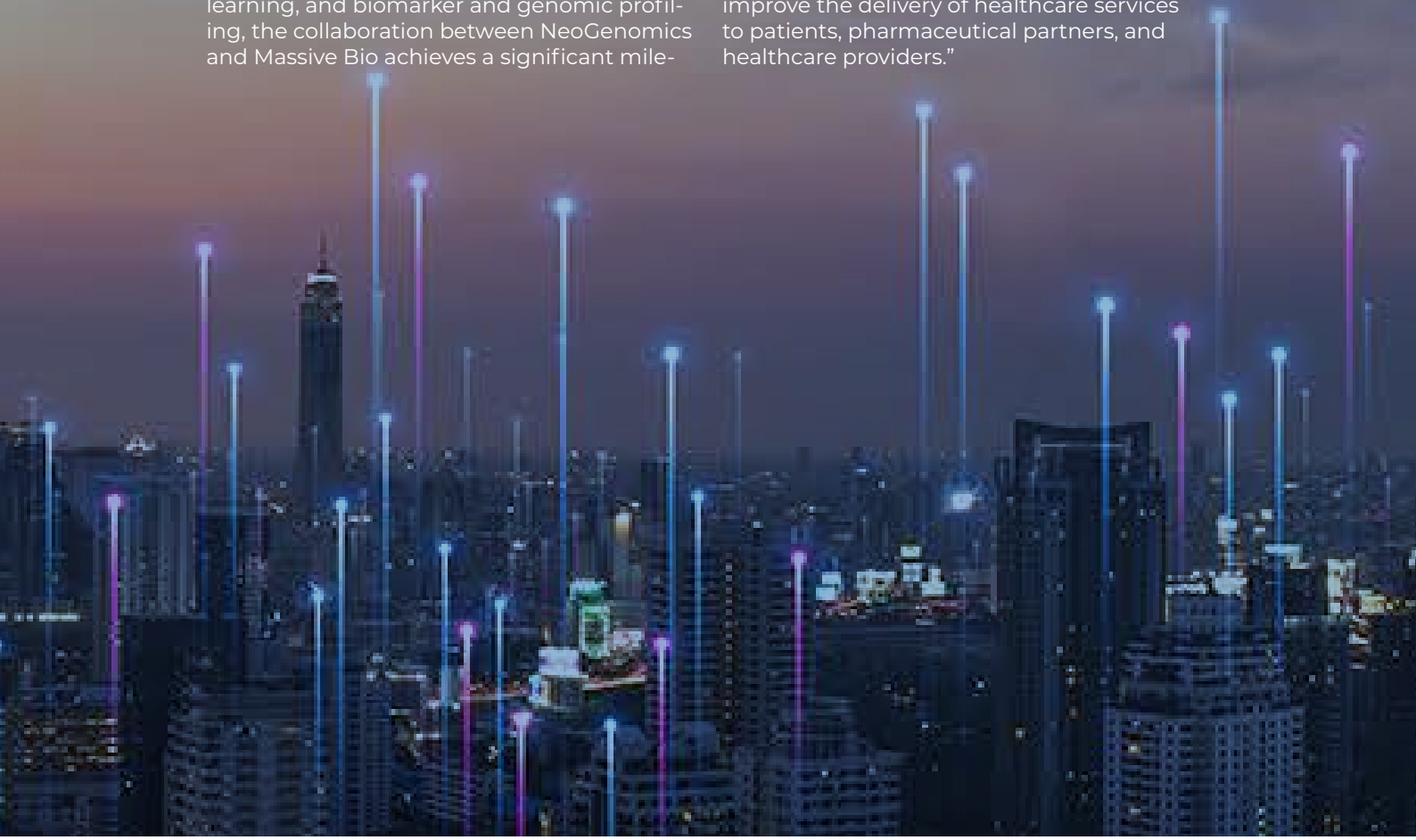
In March, Massive Bio announced a new collaboration with NeoGenomics, Inc., a leading provider of cancer-focused genetic testing services and global oncology contract research services based in Fort Myers, Florida. The goal of this new partnership: accelerating the development of new cancer therapies and ultimately improving the lives of millions of cancer patients around the world.

NeoGenomics will identify patients in real time who may be eligible for clinical trials based on biomarker status. Following initial contact and outreach provided directly from NeoGenomics to the treating physician, Massive Bio will help obtain patient consent and expedite additional screening and potential enrollment. This partnership will help to quickly identify patients eligible for clinical trials, as well as assist patients and providers in making informed decisions regarding their potential treatment avenue.

By combining their respective strengths in biomarker testing, data analysis, machine learning, and biomarker and genomic profiling, the collaboration between NeoGenomics and Massive Bio achieves a significant milestone in the oncology industry.

"Our mission at Massive Bio is to provide cancer patients with the best possible care and treatment options," said Selin Kurnaz, Ph.D. CEO and co-founder of Massive Bio. "By partnering with NeoGenomics, a leading player in the cancer diagnostics industry that shares Massive Bio's commitment to advancing cancer research and improving patient outcomes, we can leverage their expertise in oncology diagnostics to accelerate the identification of patients who may be eligible for clinical trials."

"NeoGenomics' advanced diagnostic tools and U.S. footprint, combined with Massive Bio's AI capabilities and concierge services in oncology, will enable us to match patients to clinical trials faster and more efficiently, resulting in improved outcomes and reduced costs," said Vishal Sikri, President of the Advanced Diagnostics Division of NeoGenomics. "We are thrilled to partner with Massive Bio to advance precision medicine and improve the delivery of healthcare services to patients, pharmaceutical partners, and healthcare providers."




I HAVE
CANCER
#ihavecancer #cancerawareness #massivebio

Patient Story: Jeff Shoop

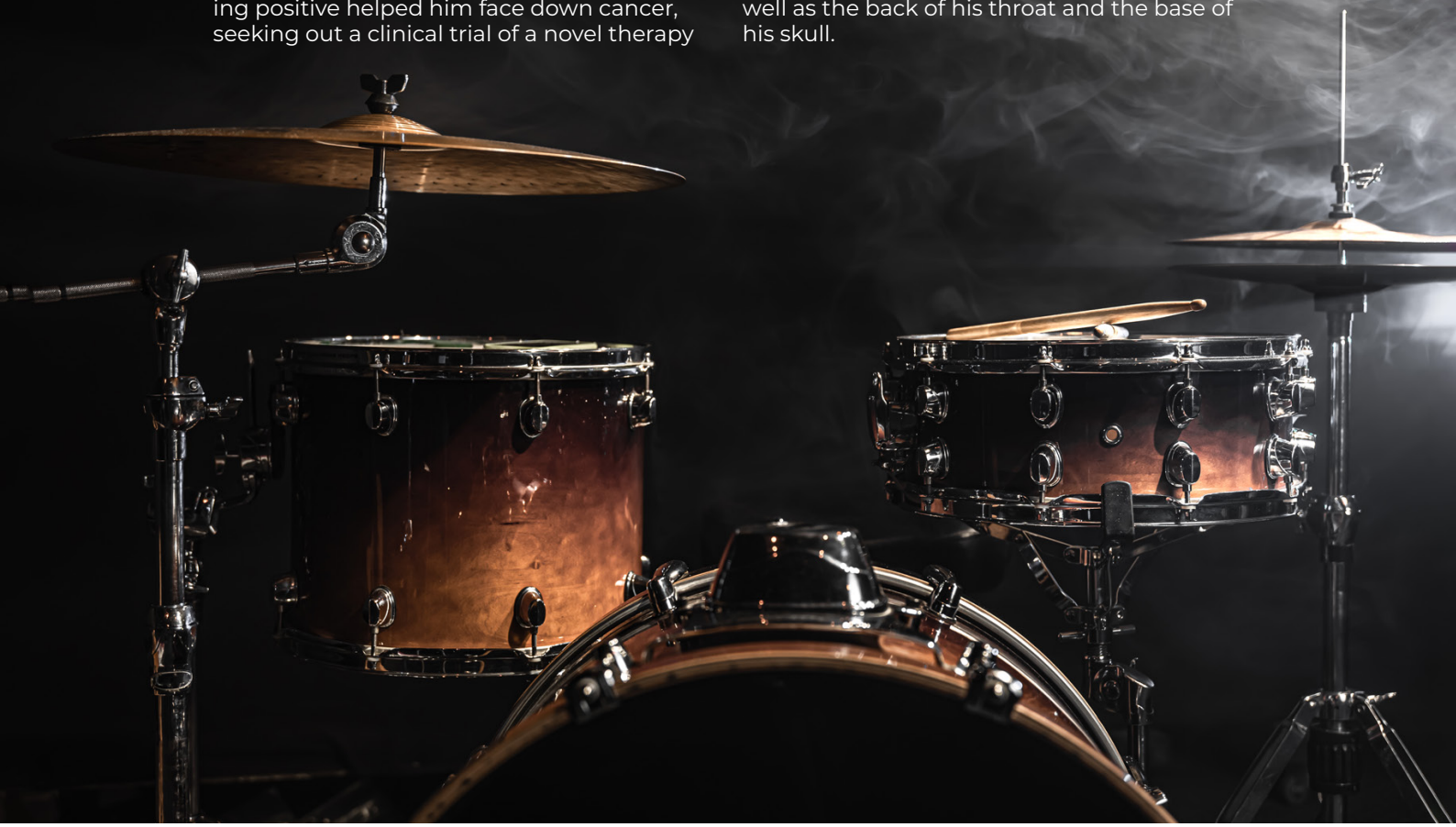
The Trial of His Life

Maintaining an upbeat attitude—and seeking out cutting-edge therapy in a clinical trial—helped drummer Jeff Shoop face down head and neck cancer

Watching drummer Jeff Shoop play bluesy country rock in the Jill Fulton Band today, you would never guess that he confronted a daunting cancer diagnosis not long ago. But Shoop, of Harrisburg, Pennsylvania, says maintaining the right attitude helped him get through the darkest days. "I have a rosy outlook on life," says Shoop, 68. "When I was getting those long chemo treatments, and the infusions, it wasn't a somber day. I'd be upbeat. I'd laugh and smile." And while staying positive helped him face down cancer, seeking out a clinical trial of a novel therapy proved critical, too.

Jeff Shoop

In 2011, Jeff was diagnosed with a form of cancer called HPV-related squamous cell carcinoma of the head and neck. He had a rectangular-shaped tumor pressing on his right nasal passage, which turned out to be causing the stuffy nose he'd had for months prior. However, Jeff's doctor told him that the cancer was stage IV, indicating that it had spread to other parts of his body—lymph nodes on both sides of his neck, as well as the back of his throat and the base of his skull.



Surgically removing the cancer would have been disfiguring, so Jeff's doctor prescribed radiation therapy and chemotherapy, which he received concurrently. The 35 courses of radiation Jeff received became more grueling with each treatment. "It hurt 24/7," he recalls. "The pain doesn't go away." Pain-relief medication helped him get through the ordeal, but the effects persisted long after he completed radiation, which caused him to develop a condition called mucositis, or inflammation of the mucous membranes, on his tongue and throughout his mouth. For several months, all he could swallow was water, so he required a feeding tube. Even tually, Jeff was able to eat food that his wife of 44 years, Lorrie, cooked, ground up, and strained. Still, his weight dropped from 220 pounds to 160 pounds.

"I had pain in my mouth for 542 days," says Jeff. "And on the 543th day, it stopped." However, he has other long-term effects from radiation treatment, including dry mouth, a common problem for survivors of head-and-neck cancer. Drinking milk or olive oil helps by coating his throat, as does chewing gum and using an oral moisturizer. He also avoids hot foods—both in temperature and spiciness—which are painful to eat. Carbonated beverages cause discomfort, too. (Otherwise, Jeff is able to maintain a normal diet today, and his weight is back up to 195 pounds.)

Chemotherapy posed a different kind of problem, since the drug Jeff's oncologist selected, cisplatin, caused him to experience major hearing loss, which is a common—and potentially permanent—side effect of the drug. "I'm a musician. I need my hearing," says Jeff, who insisted on being switched to another form of chemo, so he received cetuximab (Erbitux), instead

In 2013, Jeff joined a local chapter of a support group called SPOHNC, which stands for Support for People with Oral and Head and Neck Cancer, and is pronounced "spunk." (See page 42.) Worries about the side effects of treatment are a common topic at SPOHNC meetings, says Jeff. New members express deep concern about whether they will be able to withstand the rigors of treatment, but Jeff and other members who have been through the experience are reassuring. "The body can endure things you haven't dreamed of," he told a newly diagnosed patient at a recent SPOHNC meeting. "You're going to survive this, you're going to get through this."

When Jeff's initial cancer treatment was complete, his doctor instructed him to return once a year for a CT scan to determine if the disease had returned. "At the two-year mark, they found that I had two lumps in my right lung," says Jeff. A biopsy confirmed that the masses were cancer that had spread from his original tumor.

Lorrie & Kristin

Jeff's doctor told him that treating the newly discovered tumors with radiation wasn't an option. There is a limit to how much radiation exposure is safe for the human body, and Jeff had reached that maximum with his initial treatment. But the doctor's advice for finding a new treatment option was puzzling, at first. "Go search for clinical trials," he told Jeff and Lorrie.

"What are clinical trials?" Jeff asked. "We had a thousand questions." As he would learn, the U.S. National Library of Medicine, which is part of the National Institutes of Health, maintains a database of clinical trials, which can be accessed and searched at clinicaltrials.gov. Clinical trials, as Jeff discovered, are research studies in which scientists evaluate the benefits and safety of new therapies, including cancer drugs.

Unfortunately, searching the massive clinicaltrials.gov database—which recently listed over 95,000 cancer-related clinical trials—is an intimidating task, as Jeff discovered. "It was nuts!" he says. Jeff's mother and sister were both nurses, which means he is no stranger to medical lingo. "I've heard some of the terminology, but nothing to the degree that you need to know to get on that database and search for clinical trials. It's not patient oriented at all. It's very doctor oriented."

Despite the difficulty navigating clinicaltrials.gov, Jeff managed to find a trial that his doctor said was a perfect match. A pharmaceutical company was conducting a clinical trial of a drug called pembrolizumab (Keytruda) to learn whether it could benefit patients with

head and neck squamous cell carcinoma that had advanced after initial treatment. The trial was being held at multiple clinical sites, including Johns Hopkins Hospital, in Baltimore. Jeff contacted the trial coordinators at Hopkins and, after a bump or two in the road—delayed paperwork, a lab mix-up—Jeff ended up the last patient in the United States accepted into the trial.

For two years, Jeff and Lorrie made the 90-minute drive to Baltimore every three weeks for an infusion, plus a CT scan on some visits. "Lorrie was my rock," says Jeff, noting that his wife took notes during meetings with the doctor and team running the trial, logging answers to all of their questions about the treatment. The pembrolizumab caused Jeff some fatigue, joint pain, and other symptoms, but it had a big payoff: Jeff was one of 5 percent of patients in the trial who had a complete response, meaning that he showed no signs of cancer at the trial's end. Annual CT scans indicate that he continues to be cancer free.

Today, Jeff keeps busy playing drums with the Jill Fulton Band, which performs throughout the mid-Atlantic region of the United States, as well as with a few other groups. He also enjoys spending time with Lorrie and his family, which includes their daughter Kristin, and grandchildren, Luka, 8, and Vivian, 5.

Jeff is active in SPOHNC, serving on various panels and committees, in addition to being a member of the organization's National Survivor Volunteer Network matching program, which pairs survivors with recently diagnosed patients to share support and advice. "I try to take the 'Eeyore' aspect out of it," says Jeff, referring to the gloomy donkey character in *Winnie-the-Pooh*. "In the first year after being diagnosed with cancer, everyone tends to go to the dark side." Both one on one and in the support group setting, Jeff tries to get newly diagnosed patients to find reason for optimism. "At SPOHNC meetings, we say, 'Look around the room. There's people who have been here 25 years," he says. "That's uplifting."

And when patients who are running out of treatment options express reservations about taking part in clinical trials, Shoop is adamant. "I tell them, Look, even if it means adding two or three years of life, those are years that you will cherish," he says. "You will look back and say, I made all the right decisions."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Clinical News

Cancer Rates Drop Steeply in the United States Over the Last Generation

Earlier this year, the American Cancer Society (ACS) released its annual report on cancer facts and trends, which contained some good news: Since 1991, overall cancer deaths in the United States have dropped 33 percent. ACS officials attributed a significant portion of that steep decrease to improvements in screening and prevention of certain cancers. For example, rates of cervical cancer among women aged 20 to 24 dropped 65 percent from 2012 through 2019. That drop occurred due to the arrival of the HPV vaccine, which prevents this cancer. As acceptance of the vaccine grows, the incidence of other cancers associated with HPV (such as head and neck cancers) could decrease, too.

However, the last generation has also witnessed the arrival of new and better ways to treat many types of cancer, including immunotherapies, which stimulate the body's immune system to find and kill cancer cells; and targeted therapies, which take aim at molecules that promote cancer cells to grow and spread. Both immunotherapies and targeted therapies have been shown to improve survival of cancer patients compared to older treatments.

The news from the ACS report wasn't all good. Deaths from prostate cancer crept up 3 percent a year between 2014 and 2019. Some observers worry that changes in guidelines about screening for prostate cancer have led many men to skip standard tests that can detect the disease early, such as the prostate specific antigen (PSA) assay, which has resulted in many cases going undiagnosed until they have spread beyond the prostate, making them difficult to treat.

Fortunately, researchers continue to discover new weaknesses in cancer's armor, and work in labs and in clinical trials continues to produce new therapies that will help drive down cancer mortality.

Vaccine Shows Promise for Triple-Negative Breast Cancer

Triple-negative breast cancer has long frustrated patients, doctors, and drug developers. These tumors are so named because they lack receptors for estrogen and progesterone, which are hormones, as well as a protein called HER2. Blocking estrogen, progesterone, and HER2 with medication slows the growth of most breast tumors, but about 15 percent of breast cancer cases don't respond to these drugs, which limits treatment options. Now the results of a promising new study suggest that a vaccine might one day be a new option for triple-negative breast cancer.

In a phase 2 clinical trial published in *Nature Medicine*, researchers injected a drug called talimogene laherparepvec (Imlygic) into the tumors of 37 patients with stage II and stage III triple-negative breast cancer who were also receiving chemotherapy, and who later had surgery to remove the tumors. Talimogene laherparepvec is an oncolytic vaccine; unlike vaccines for preventing diseases such as COVID-19 and the flu, these vaccines are designed to infect and kill cancer cells. They also appear to stimulate the body's immune system to join the attack on malignant tumors. Among the vaccine recipients, 45.9 percent had a complete response, meaning they had no sign of cancer after surgery, while eight more had only a few cancer cells remaining. After two years, 89 percent of the patients were cancer free. Talimogene laherparepvec is already approved for treating advanced melanoma. Next, researchers will conduct a phase 3 study to confirm whether this vaccine offers a much-needed new treatment option for triple-negative breast cancer.

Phase 2 Trial of New Biomarker-Based Therapy Shows Promise for Certain Forms of Esophageal Cancer

The biomarker HER2 is commonly associated with breast cancer, but excessive levels of this protein can also promote the growth and spread of malignant cells in a subset of eso-

phageal cancers, known as cancers of the gastroesophageal junction which is the meeting place between the esophagus and stomach. A few drugs are available for treating gastroesophageal junction tumors that test positive for HER2, and a new one may soon join them.

In a phase 2 study, researchers evaluated an experimental drug called zanidatamab combined with chemotherapy as an initial treatment for patients with advanced gastroesophageal cancer (specifically, the form known as adenocarcinoma) that tested positive for HER2 and had metastasized, or spread to other organs. Zanidatamab is a bispecific antibody, meaning that it attaches to HER2 proteins in two different locations. A total of 46 patients from the United States, Canada, and South Korea took part, and all received zanidatamab and chemotherapy.

As they reported at the 2023 ASCO Gastrointestinal Cancers Symposium, the researchers found that 84 percent of participants survived at least 18 months. The median overall survival could not be determined because after 26.5 months, more than half of the patients had survived. The disease control rate—that is, the percentage of patients who had a complete or partial response to treatment and had stable disease—was 92 percent. A phase 3 trial is underway that will study zanidatamab combined with chemotherapy, with or without an experimental therapy called tislelizumab, in a larger group of patients.

New Approval: Zanubrutinib for CLL or SLL

In January, the U.S. Food and Drug Administration (FDA) approved zanubrutinib (Brukinsa) for the treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). The FDA based its approval on the results of a clinical trial called SEQUOIA, which included patients with CLL and SLL who had not yet received treatment, as well as the ALPINE trial, which included patients with CLL or SLL that had returned after treatment (relapsed) or failed to respond to treatment (called refractory disease).

In ALPINE, the larger of the two studies, 327 patients were randomly selected to receive zanubrutinib, while another 325 patients received ibrutinib (Imbruvica). Patients were treated until their cancer worsened or they couldn't tolerate the drugs' side effects. An independent review committee found that 80 percent of patients treated with zanubrutinib responded to the drug, compared to 73 percent given ibrutinib. The typical (or median) duration of response in patients given the latter drug was about 14 months. By comparison, median duration of response for those treated with zanubrutinib could not be determined, since more than half were still having an adequate response when the study period ended. SEQUOIA, which compared zanubrutinib to the combination of bendamustine (Treanda) plus rituximab (Rituxan and others), reached a similar finding.


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Are You Getting the **Best Treatment?**

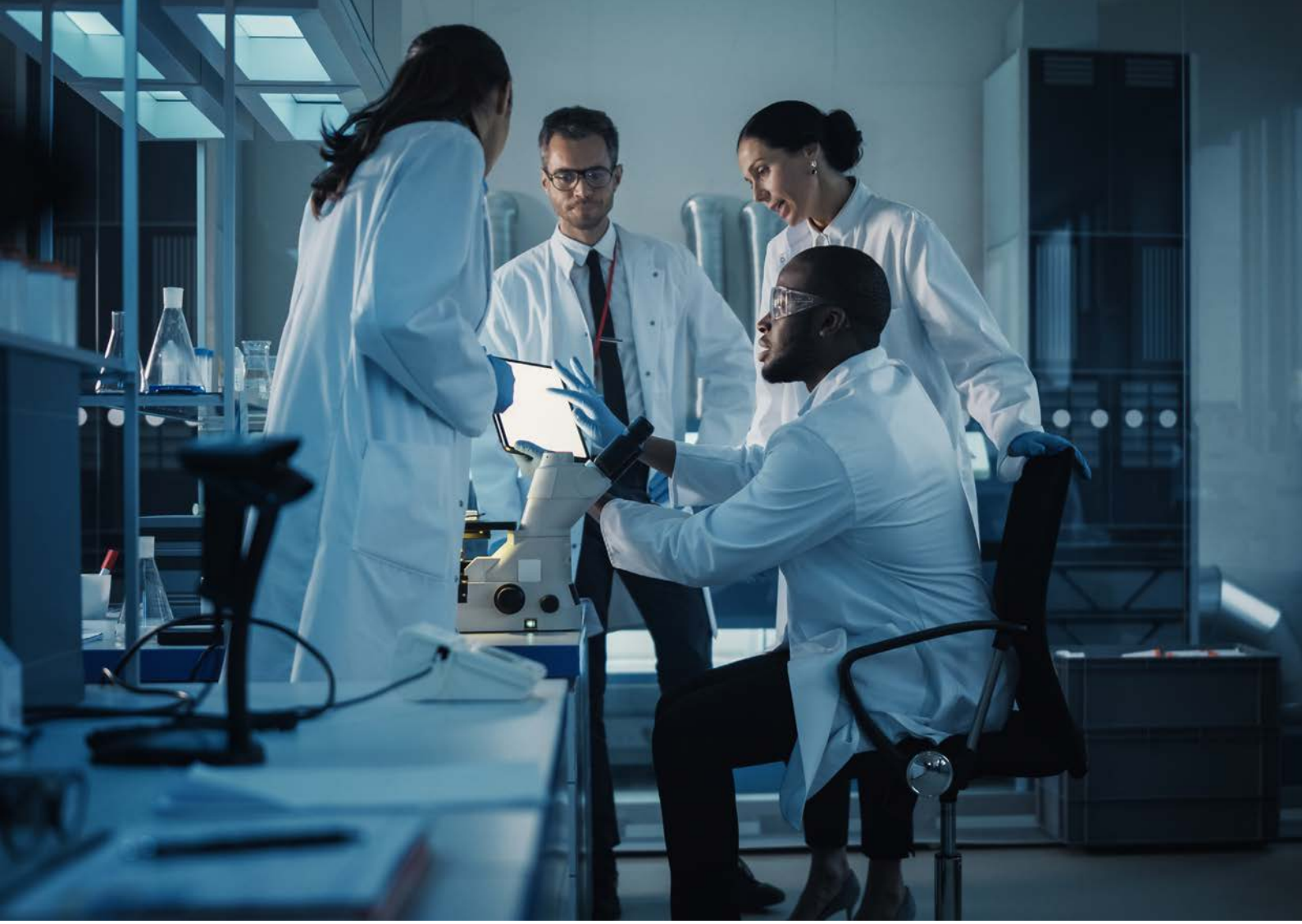
Many new cancer therapies are approved every year, but research indicates that not all patients have equal access to the latest breakthroughs. How can you be sure you're getting the most-advanced treatment?

Every cancer patient has a right to expect the most effective and up-to-date treatment for his or her condition. Regrettably, some people with cancer don't receive the latest therapies, which often offer better outcomes than older treatments. Taking certain steps can help give you confidence that you're receiving the best treatment available.

Unequal access

A study published earlier this year in *JAMA Oncology* underscored the unfortunate reality that a significant portion of cancer patients who could benefit from innovative, newly approved treatments don't get them. In the study, investigators examined 71,659 Medicare claims from 1732 oncology clinics to determine whether the practices adopted immunotherapy treatments for cancer patients within two years of the drugs' approval by the Food and Drug Administration. The various forms of immunotherapy now available for treating many different types of cancer have been major breakthroughs, as they train the body's immune system to recognize and destroy cancer cells. Studies indicate that immunotherapies can prolong survival compared to standard treatments, often with fewer side effects.

Yet, the *JAMA Oncology* study showed that adoption of these potent medicines has been uneven in the United States. Researchers found that practices in rural parts of the country were 11 percentage points less likely than urban-based practices to offer newly approved immunotherapy treatments to their patients. Small practices were less likely



to be up to date, too: Those with one to five physicians had adoption rates that were 27 percentage points lower than in practices with six or more doctors. Independent and nonacademic practices had similar rates of prescribing the new immunotherapies, but both were lower than academic medical systems.

Earlier studies reached similar conclusions: Not all cancer patients are treated equally, with some lacking access to the latest—and often best—treatments. That's particularly frustrating given that drug developers are producing new oncology therapies at an unprecedented pace. In 2021 alone, a record 30 new cancer treatments were introduced around the world.

What causes the treatment gap?

Why don't some cancer patients receive the latest treatments? Experts say there are several reasons that doctors in all areas of medicine might be slow to embrace new treatment approaches. Some may be too busy caring for patients to read medical journals and attend conferences, which would help them become aware of the benefits of new theraies. Other physicians suffer from "practice inertia," that is, they are reluctant to change how they have always treated patients with a given disease. In some cases, doctors may fear that a new treatment will incur excessively high costs for patients. In the United States, where even patients who have medical insurance are often required to contribute toward the price of treatment, out-of-pocket expenses for cancer patients can run as high as $2600 a month, according to a 2021 study in *Current Oncology*.

And there may be more troubling reasons for unequal access to the latest cancer treatments. According to a 2021 editorial in *JAMA Oncology*, fewer than half of patients with stage IV melanoma receive immunotherapy, while the same is true for just 8.7 percent of patients with stage IV non-small cell lung cancer. Meanwhile, just 40 to 52 percent of women with breast cancer who were candidates for immune-based treatments received them. Yet, national guidelines recommend immunotherapy for treating each of these cancers.

The authors of the *JAMA Oncology* editorial argued that, in addition to cost, another factor that likely results in the underuse of these therapies is racial bias. They note that Black patients with melanoma wait longer than non-Hispanic white patients to receive immunotherapy, for example, and that Black

patients with non-small cell lung cancer are less likely than white patients to be offered immunotherapy at all. Meanwhile, one study found that Black women with breast cancer who are eligible to receive the drug Herceptin are less likely than other patients to be offered the drug. Other factors that appear to reduce the likelihood of receiving immunotherapy include living in a community with low education levels and having Medicaid or no insurance.

How to get the best treatment

A good first step toward making sure you get the right treatment is to work closely with your doctor and treatment team, says oncologist Arturo Loaiza-Bonilla, MD, co-founder and chief medical officer of Massive Bio. "They will assess your individual case and consider various factors such as the type and stage of cancer, your overall health, and potential side effects before making a recommendation for treatment," says Dr. Loaiza-Bonilla. Cooperating fully and providing as much information as possible about your symptoms and any side effects that you experience can help your team pick the right treatment for you.

Other steps to take include:

• **Educate yourself.** Learning all you can about your cancer, including how expert physicians recommend treating it, is essential. The National Comprehensive Cancer Network publishes excellent guidelines for the treatment of many types of cancer for patients that are written in plain, easy-to-understand English. Try to keep up to date with current research on treatments. One way to do that is to set up a Google Alert with the name of your cancer and keywords and phrases such as "treatment," "Food and Drug Administration," and "drug approval."

• **Have a frank conversation with your physician.** If you think for any reason that you may not be getting the optimal therapy, ask your doctor to explain how he or she devised your treatment plan. If it doesn't include a medication or other therapy you think you should be taking based on your research, ask why.

• **Consider seeking a second opinion.** Many patients are reluctant to do so, out of fear that they will offend their doctor. However, seeking second opinions is common and most doctors are not only comfortable with the idea, but will suggest another clinician to seek out for his or her perspective.

Finally, you can gain access to the latest therapies by enrolling in a clinical trial, in which researchers evaluate innovative new treatments. Massive Bio specializes in helping people with cancer find and enroll in clinical trials of potentially life-changing, and even lifesaving, therapies. Our team of oncology nurses and patient advocates is standing by to help.

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An Interview with **Cagatay Culcuoglu**

Massive Bio Co-Founder Cagatay Culcuoglu is the company's chief operations officer and chief technology officer. He spoke with us about how Massive Bio is using artificial intelligence in new ways to help cancer patients find hope.

Q: Before we talk about technology, could you tell us a bit about the origins of Massive Bio?
A: Massive Bio was founded in 2015 by three entrepreneurs—Dr. Selin Kurnaz, Dr. Arturo Loaiza-Bonilla, and me—with the mission of making precision oncology accessible to all cancer patients in the United States. Both Dr. Kurnaz and I were caregivers to close family members who had cancer and met with Dr. Loaiza-Bonilla. We observed how challenging it is for cancer patients and caregivers to access quality care. We developed a cloud-based platform that connects oncologists to a network of world-renowned cancer genomics experts, allowing them to access the most advanced genetic testing and provide the best possible care to their patients. We built a proprietary algorithm and database to analyze patient data and provide personalized genomic insights to inform treatment decisions, clinical trial options, and access to suitable drugs.

Q: How did you go about building the technology that would eventually become SYNERGY-AI, Massive Bio's clinical trial matching platform? What did that require?
A: We built the technology that became SYNERGY-AI by utilizing artificial intelligence (AI) and machine learning to analyze patient data and generate personalized therapeutic recommendations. This required leveraging proprietary algorithms and a deep understanding of biological pathways, drug targets, and drug interactions. Additionally, the team had to build an extensive library of patient data and use that to develop and continually refine their algorithms. Finally, the system had to be designed to be accessible and intuitive for healthcare professionals and their patients, which required an intuitive user interface and an easy-to-follow workflow.

Q: How does SYNERGY-AI take a patient's medical data and identify matching clinical trials?
A: Massive Bio's platform utilizes a combination of medical expertise and technology to match patients with clinical trials. The patient's medical data, including lab results and medical history, is initially reviewed by our proprietary AI solution. This software is then employed to compare this data to the current enrolling clinical trial criteria. Matches are identified through the software, and medical experts evaluate the appropriateness of the trials for the patients. Finally, a list of clinical trials that match the patient's data is presented to them. We also track the result and update our machine-learning systems

to continue to expand our recommendation capabilities. Overall, this platform is a useful resource for patients seeking access to clinical trials or drugs, as it simplifies the process and ensures the appropriateness of matches through a combination of technology and medical expertise.

Q: Is the trial-matching platform a "finished product" or are you constantly modifying it? If so, how? What kinds of changes or improvements have you made recently?
A: We are constantly making improvements and adding new features to the platform as the complexity of cancer cases increases, new drugs become available, and biomarker- and genomic-related diagnoses become more available. This makes it easier to use and more intuitive for our users. Recently, we have added a new feature that allows users to search for trials by condition, location, or provider, as well as several additional filters to narrow down the results. We have also improved the search capabilities to allow for more specific results. Additionally, we have added several new patient-education resources to help our users make informed decisions about their care. Finally, we have made several design improvements to our platform to make it easier to navigate and to provide a better user experience.

Q: Describe the team that develops and maintains the technology platform. Who are they and what do they do?
A: The multidisciplinary team developing and maintaining the Massive Bio technology platform is comprised of approximately 20 people. This team is composed of software engineers, data scientists, software architects, product managers, oncology/hematology nurses, physicians, and customer service representatives. The software engineers are responsible for developing and maintaining the platform, while the data scientists ensure the data is secure, accurate, and up to date. The software architects are responsible for ensuring the platform is designed and built to scale and meets customer needs. The product managers are responsible for managing the product roadmap and ensuring that customer requirements are met. Finally, the customer service representatives provide support to individuals and help troubleshoot any issues.

Q: Massive Bio is rolling out a drug-matching platform. How did that idea come about?
A: The idea for the drug-matching platform came about in response to the growing demand for more comprehensive and personalized medical care, and we saw it as a way to address this need. Creating a platform where biotech and pharmaceutical companies can better target which patients and physicians need the latest drugs improves their go-to-market efficiency. This new product will build on the company's existing AI platform, which is focused on oncology and has already facilitated clinical trial matching services for more than 100,000 patients.

Q: When and how did the idea for the drug-matching platform come about?
A: We first had the idea for a drug-matching service in early 2020 when COVID-19 became predominant globally. We were working with the team to expand our SYNERGY-AI clinical trial matching capabilities. However, we realized that due to mobility issues, clinical trial enrollment and access to most relevant drugs took a hit, and that pharmaceutical companies faced new challenges. We wanted to make it easier for people to find the best medication for their needs and decided to create a matching service that would

provide personalized recommendations for medications based on individual patient profiles.

Q: What other benefits will the drug-matching platform offer?
A: Our AI technology also improves equity and access to oncology care, providing trial options, value-based pathways, and a framework for payers to authorize treatments, which will promote adherence and reduce costs. These therapies need to be reimbursed to prevent financial toxicity, and insurance companies and providers need reassurance that there is a digital tool in place to allow precision oncology and value-based matching. Instead of the current data-poor environment, where patients get less individualized, yet more expensive, treatment options, our matching platform can identify a pathways-oriented, value-based, biomarker-driven agent, in addition to clinical trial options. We are that best-in-class solution.

Q: What do you hope this new platform will achieve?
A: By using AI, the platform helps cancer patients identify relevant clinical trials, resulting in faster access to treatment options. Additionally, the platform enables life sciences companies to conduct recruitment more inclusively, beyond traditional site-specific recruitment.

Furthermore, the platform removes logistical constraints for patients once they are matched to a specific treatment, which increases the chances of successful treatment outcomes. The new product aims to expand upon these benefits and improve patient care and treatment options by further enhancing the use of AI in oncology.

Q: How do you see AI changing people's lives for the better in the future?
A: AI in healthcare can be seen as a potential tool to help reduce the cost of healthcare, improve the accuracy and speed of diagnosis, and provide personalized treatments for patients. AI can be used to analyze medical data, identify patterns, and provide personalized recommendations for treatments. AI can also be used to help automate administrative tasks, such as scheduling appointments, tracking patient information, and managing medical records. AI can also help spot potential health risks, such as identifying a patient's genetic predispositions for certain diseases. AI can also be used to improve medical imaging and diagnostics, as well as provide insights into medical research.

AI-powered healthcare could help diagnose and treat illnesses more accurately and quickly. AI could also be used to make transportation safer and more efficient for patients and caregivers, and to create personalized learning experiences. Finally, AI could help reduce poverty and inequality by creating new opportunities for people in underdeveloped nations.

Artificial Intelligence

Technology of Massive Bio

Biomarkers 101

Biomarkers are transforming the way cancer is diagnosed and treated—but what exactly are they? Here's what you need to know about biomarkers if you or a loved one has cancer.

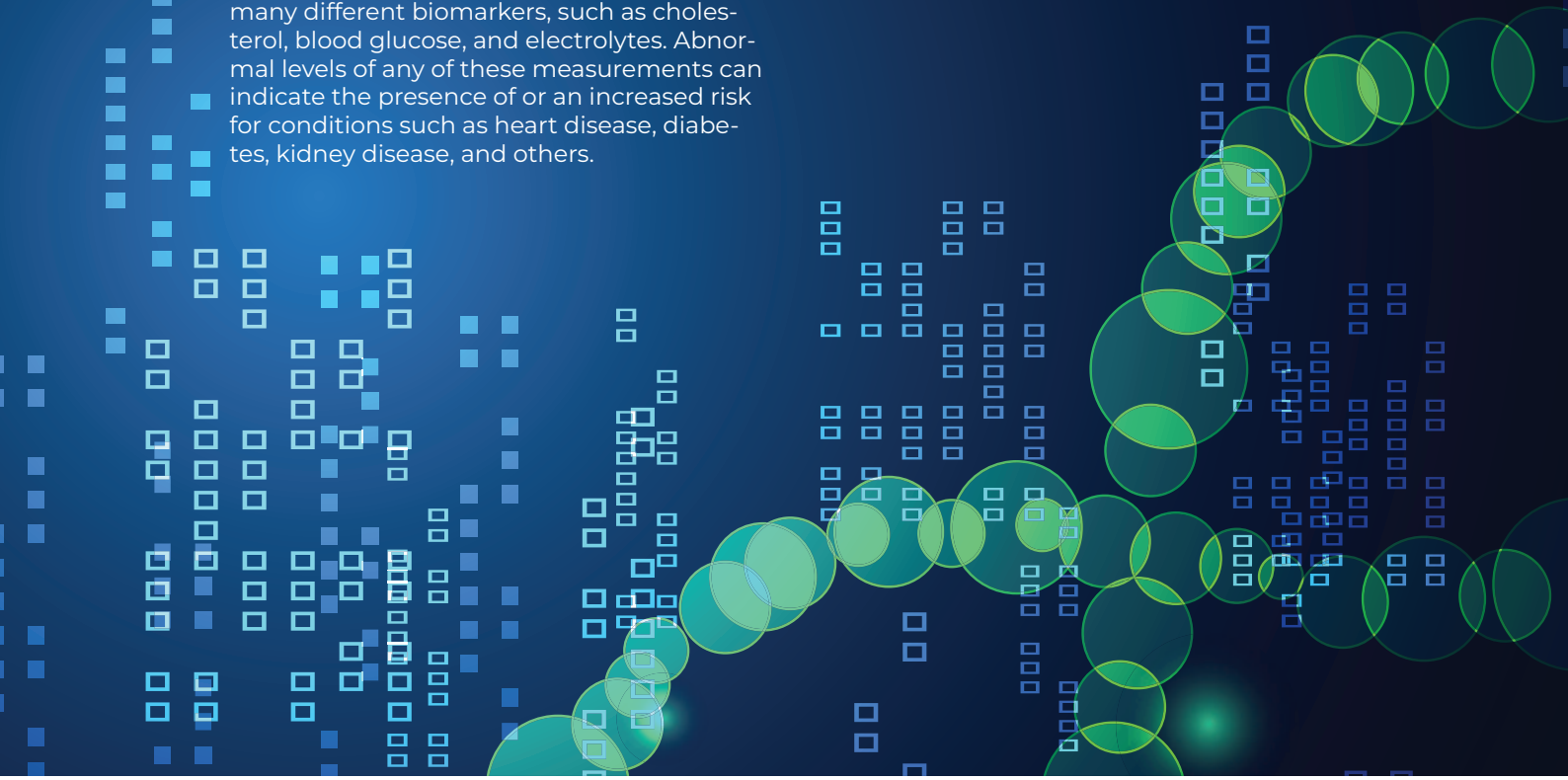
Doctors who treat people with cancer are constantly searching for new tools and strategies to help their patients live longer and enjoy better quality of life. In recent years, cancer biomarkers have emerged as prime targets for treating certain forms of cancer. In fact, drugs that target specific biomarkers have become the standard of care for many types of tumors. As scientists learn more about what makes malignant cells grow and spread, biomarkers are destined to play an increasingly important role in cancer care.

A biomarker is any aspect of your health that can be measured with a test. Using biomarkers to diagnose and treat disease is hardly a new idea. Your doctor probably checks your blood pressure at most office visits—that's a biomarker, since high blood pressure increases the risk for many medical conditions, but can be lowered with medication and lifestyle changes. The routine blood test that's part of your annual physical exam includes many different biomarkers, such as cholesterol, blood glucose, and electrolytes. Abnormal levels of any of these measurements can indicate the presence of or an increased risk for conditions such as heart disease, diabetes, kidney disease, and others.

Cancer biomarkers are genes, proteins, and other molecules that can provide information about a patient's tumor, such as whether it's likely to spread (or metastasize) slowly or aggressively. Researchers have identified many cancer biomarkers, and more are being discovered with each passing day in labs around the world. Not all forms of cancer have known biomarkers. What's more, two people can have the same type of cancer, such as breast cancer, but tests may show that one has established biomarkers for the disease, while the other does not. Knowing a patient's biomarker status can have an important impact on treatment choices, as you will see.

Cancer biomarkers: Screening and targeting

Cancer biomarkers may be measured in some patients for several reasons. For starters, biomarkers can be used in screening patients for certain types of cancer. Screening



is routine testing of people who don't have symptoms to determine if they have a disease, which increases the chances of catching it early, when it's most treatable. One of the earliest forms of biomarker screening for cancer was the prostate specific antigen (PSA) test, which was first approved by the U.S. Food and Drug Administration in 1986 and can detect a protein that may rise in the blood of men who have prostate cancer. The test was initially approved for monitoring how patients respond to treatment for prostate cancer, but is now widely used as a screening tool to identify men who may have the disease, who can be referred for further testing.

However, cancer biomarkers are increasingly used to guide treatment decisions, thanks to the rise of precision (or personalized) medicine. The concept of precision medicine is based on a simple idea: No two patients are alike, so their individual characteristics should be considered when making treatment decisions. As mentioned earlier, that's true even when two patients have the same form of cancer, such as breast cancer—there are different biological mechanisms that cause breast cells to begin growing uncontrollably, form tumors, and spread throughout the body. As a result, the treatment most likely to shrink a tumor in one patient may offer no benefit to another. That became clear when scientists discovered that about 20 percent of women with breast cancer have an unusually aggressive form because they produce a protein called HER2 that makes cancer cells grow faster. That discovery led to the development of Herceptin, which is sometimes called the first form of personalized medicine and was approved for women with HER2-positive breast cancer in 1998. Women with breast cancer are now routinely tested for the HER2 biomarker.

In the ensuing years, researchers have identified many other cancer biomarkers, and some have been used as "targets" for new oncology drugs. For example, two of the earliest cancer biomarkers discovered were the BRCA1 and BRCA2 genes; women who are born with mutations, or alterations, in these gene have a significantly increased risk for breast cancer and ovarian cancer. However, scientists later discovered that targeted therapies called PARP inhibitors can improve survival in some breast cancer patients who have BRCA mutations.

Here is a small sampling of other cancer biomarkers that can make certain patients candidates for cutting-edge targeted therapies, which may be combined with chemotherapy:

• BRAF gene mutation, in colon cancer, melanoma, and non-small cell lung cancer.

• EGFR gene mutation, in lung cancer.
• KRAS gene mutation, in colon cancer and non-small cell lung cancer.
• NTRK gene, which can undergo a change called “fusion” and can play a role in many different forms of cancer.

What’s more, some forms of immunotherapy—which strengthens the body’s natural defense system, making it better able to detect and kill cancer cells—target certain cancer biomarkers, too. For example, some cancer cells produce large amounts of a protein called PD-L1, which causes protective T cells to “turn off,” which prevents them from hunting down and destroying tumors. If tests show that a cancer patient has high levels of PD-L1, he or she may be a candidate for a form of immunotherapy called a checkpoint inhibitor, which blocks PD-L1, allowing T cells to return to finding and killing cancer cells. One example is the drug pembrolizumab (Keytruda), which is approved for treating patients who test positive for elevated PD-L1 and have specific forms of lung cancer, head and neck cancers, esophageal cancer, and cervical cancer. Other checkpoint inhibitors target additional proteins that cause cancer to grow and spread.

How are biomarkers tested?

There are several ways to measure cancer biomarkers, including:
• Blood tests, though other fluids such as saliva may be used.
• Biopsies, which use fine needles inserted beneath the skin to obtain tumor tissue samples.
• If you had surgery to remove a tumor, tissues from it can be tested for biomarkers.

Blood or tissue samples are sent to a lab, where they are analyzed to determine if they carry biomarkers that a doctor suspects could be involved in a patient’s cancer. Not all hospitals or medical clinics are equipped to perform testing for cancer biomarkers, so if your doctor thinks you could benefit, you may need to visit a lab or other medical facility.

If you have cancer, ask your doctor if you are a candidate for biomarker testing and, potentially, biomarker-based therapy. (Biomarker testing is sometimes called molecular testing, genomic profiling, and tumor profiling, among other names.) If not, it’s possible that there is a clinical trial underway near you that’s evaluating a novel biomarker for your type of cancer. In fact, one recent report showed that more than half of all cancer clinical trials currently being conducted involve the use of biomarkers. Massive Bio specializes in matching cancer patients to clinical trials of promising new therapies—contact us at support@massivebio.com or +1 (844) 627-7246 to learn more.


IF YOU'VE BEEN DIAGNOSED WITH CANCER AND HAVE A SPECIFIC MUTATION,
innovative clinical trials are now enrolling near you.
ACT NOW!

Update on **Esophageal Cancer**

Esophageal cancer is on the rise in some populations. Fortunately, effective new treatments have arrived and more innovative medicines are on the way.

April is Esophageal Cancer Awareness Month. Recent research suggests that this disease is transforming in several important ways. For one, doctors are diagnosing esophageal cancer more often in groups of patients who infrequently developed the condition in the past, and the disease's incidence is rising in some parts of the world. What's more, there are two major forms of esophageal cancer, and the type of malignancy diagnosed most often is changing around the globe. These two trends appear to be intertwined.

Fortunately, researchers are working diligently to discover new therapies for esophageal cancer, which can be challenging to treat if it isn't discovered at an early stage. New medicines have become available recently, though not all patients can benefit from them, so the search for innovative approaches to treating esophageal cancer continues.

A surprising rise

Esophageal cancer typically afflicts older men and women, but studies show that it's becoming more common in younger people. In the United States, people aged 65 to 74 make up the biggest group of esophageal cancer patients. Overall, rates of esophageal cancer have been trending downward in the country over the last generation or so. However, the portion of people aged 45 to 64 who were diagnosed with this cancer in the United States nearly doubled between 2012 and 2019, according to an analysis of five million patient records that was presented at a medical conference in 2022. The analysis also found that the portion of people in the 45-

to-64 age group who were diagnosed with Barrett's esophagus—a condition that often precedes esophageal cancer—rose 50 percent during the same period. In some cases, a spike in cancer diagnoses can occur over time because doctors acquire better tools for screening and detecting a given disease. However, the authors of the study ruled that out as a possible cause of the rise in esophageal cancer and Barrett's esophagus in this younger population.

The incidence of esophageal cancer has risen in other parts of the world, too. A 2021 study in the journal *Cancer Causes & Control* found that cases of and deaths from esophageal cancer rose in China, Japan, and South Korea from 1990 to 2017, for example. What's causing esophageal cancer to rise in some groups? Experts say that two major contributors are gastroesophageal reflux disease, or GERD, and obesity, which are both becoming more common. GERD, or chronic heartburn, occurs when stomach acid leaks upward and into the esophagus, where it can damage tissue and cause a lesion (or tissue injury) to form. Over time, untreated GERD can cause Barrett's esophagus, which increases the risk for the form of esophageal cancer called adenocarcinoma. There has been a significant increase in GERD in some countries recently, including the United States.

Obesity, which is a growing global health threat (over 40 percent of the U.S. population is obese), increases the risk for developing GERD and is also closely associated with adenocarcinoma. At one time, another form of esophageal cancer, called squamous cell carcinoma, was by far the most common type around the world. But as waistlines get wider, adenocarcinoma is becoming more prevalent, too.

New treatments for advanced esophageal cancer

Both forms of esophageal cancer can be difficult to treat, especially when they're detected at advanced stages. However, the prospects for people with esophageal cancer are significantly more promising today than in the past. As recently as the 1970s, patients diagnosed with esophageal cancer had just a 5 percent chance of living another five years, on average. Today, that figure has quadrupled, to 20 percent.

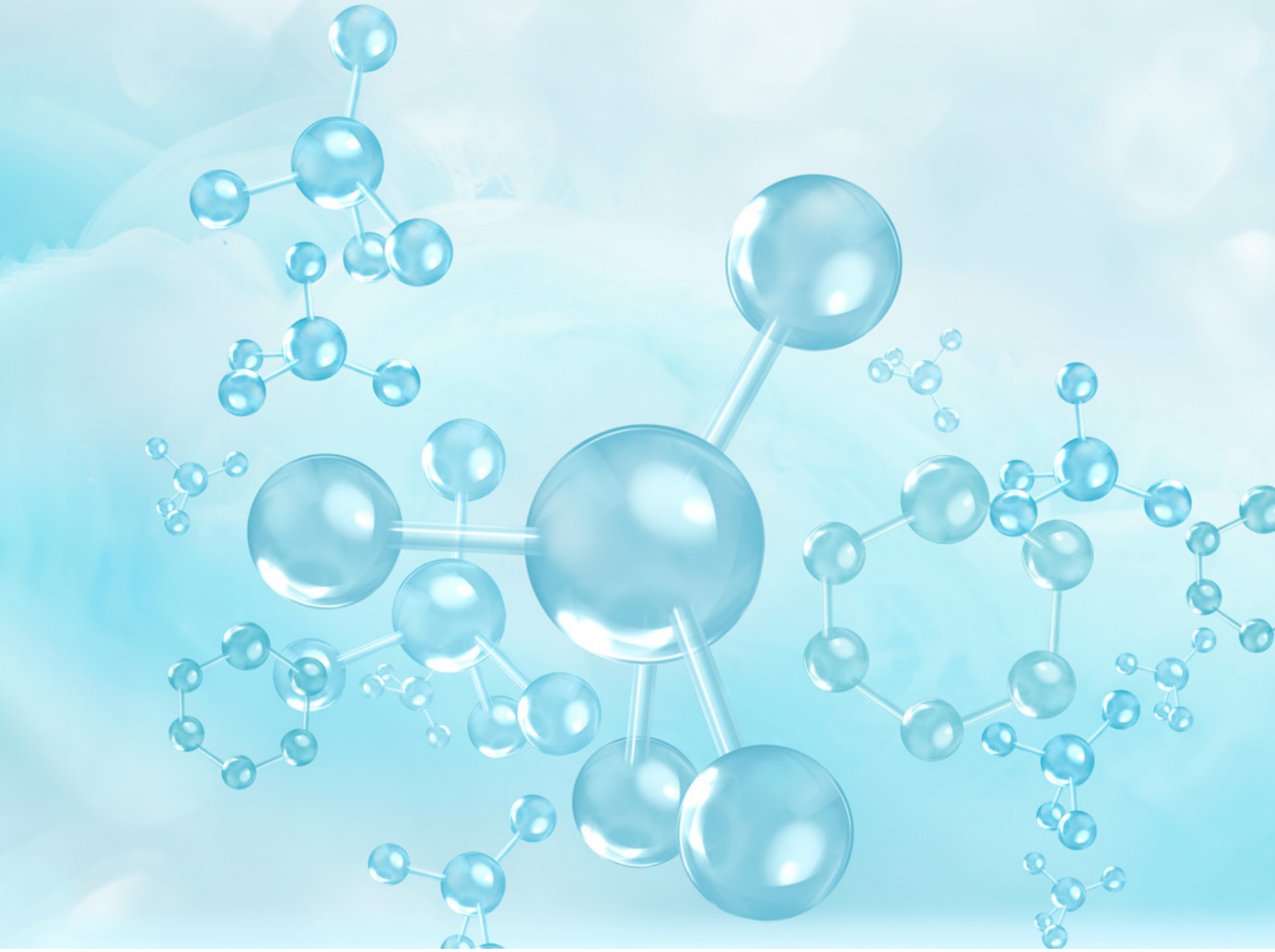
The improvements in survival may be partly explained by lifestyle changes that have occurred over the last few generations. For example, smoking not only increases the risk for esophageal squamous cell carcinoma, but current and former smokers who are diagnosed have a worse prognosis (or outlook) than patients who never smoked, according to research. Smoking rates have plummeted in many countries in recent years, which means fewer patients who develop squa-

mous cell carcinoma have the disadvantage of a history of tobacco use, and may live longer with the disease as a result.

However, the arrival of better treatments for esophageal cancer has undoubtedly contributed to improvements in survival. At early stages, before it has spread to other tissues, esophageal cancer is typically treated with surgery (or other procedures to remove a tumor), chemotherapy, and radiation. However, some patients with more advanced cases of esophageal cancer or who can't have surgery or chemotherapy may be candidates for effective new drugs that have been shown in studies to help people with advanced esophageal cancer live longer.

One group of innovative medicines to become available in recent years is known as targeted therapy. Unlike chemotherapy, which can harm both malignant and healthy cells, targeted therapies take aim at specific gene mutations, proteins, and other molecules that promote the growth and spread of cancer cells. Targeted therapies for esophageal cancer include:

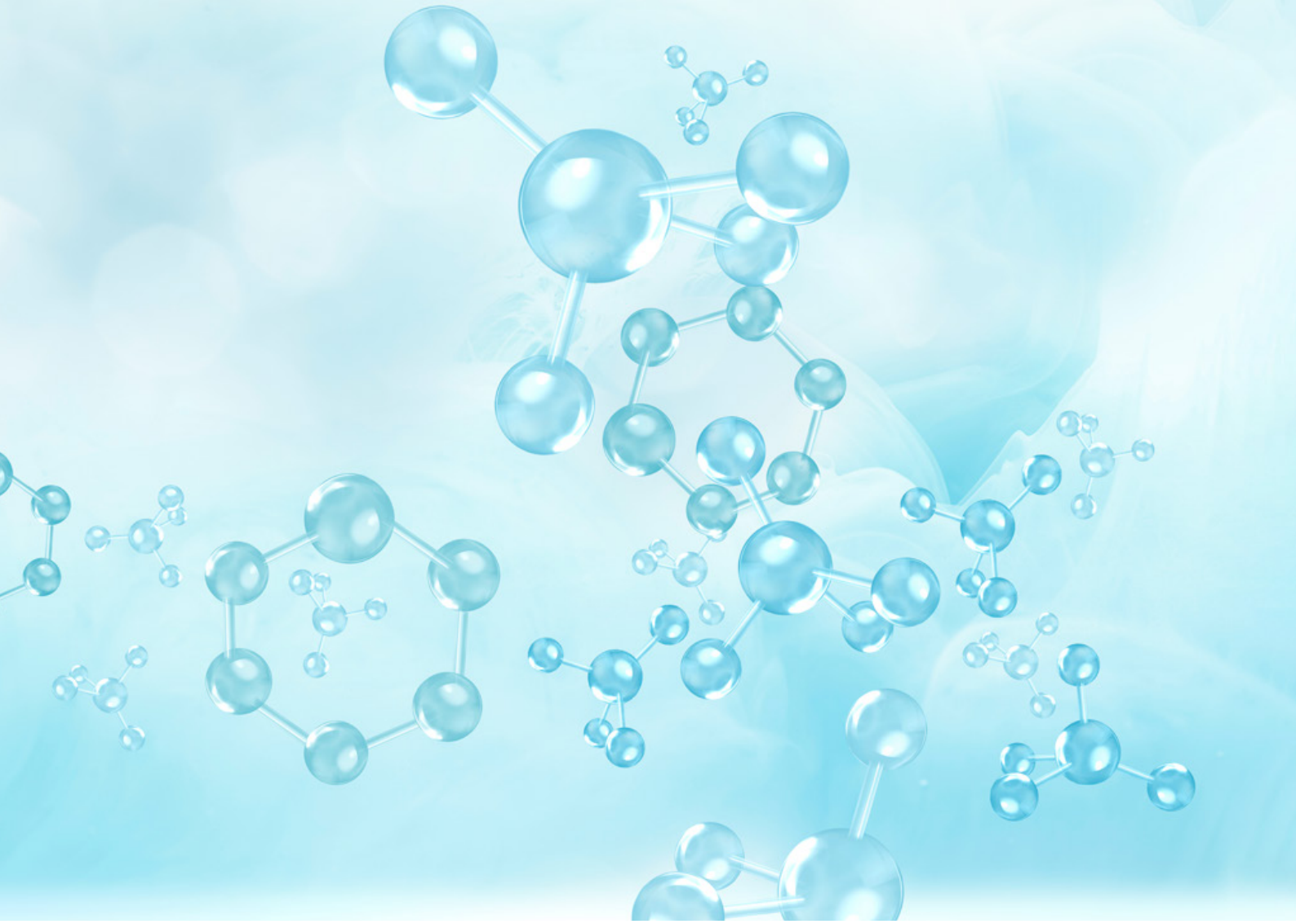
- **Trastuzumab (Herceptin and others) and trastuzumab deruxtecan (Enhertu):** These drugs target a protein called HER2, which promotes tumor growth and is increased in some patients with esophageal cancer. (HER2 is elevated in some other cancers, including certain cases of breast cancer.)
- **Ramucirumab (Cyramza):** Like healthy cells, cancer cells require blood and nutrients to survive. This drug blocks a protein called VEGF that's necessary for the formation of blood vessels that deliver blood and nutrition to cancer cells.
- **Entrectinib (Rozlytrek) and larotrectinib (Vitrakvi):** While many cancers are caused by mutations, or alterations, in genes, others occur when genes attach, or fuse, to other genes. A gene called NTRK sometimes fuses with others and sets the stage for certain cancers, including esophageal cancer. These drugs can slow or stop the uncontrolled cell growth that can arise from this gene fusion.



Another important new form of treatment for esophageal cancer is called immunotherapy, which trains the body's immune system to find and destroy cancer cells more effectively. The type of immunotherapy used to treat esophageal and many other forms of cancer today is known as an immune checkpoint inhibitor. Cancer cells have various strategies for evading detection by the immune system. One is to produce proteins that turn protective T cells to the "off" position, so they won't attack cancer cells. Immune checkpoint inhibitors flip T cells back into the "on" position so they can detect and lead an assault on cancer cells. Immune checkpoint inhibitors that may be offered to treat advanced esophageal cancer include:

• **Pembrolizumab (Keytruda) and nivolumab (Opdivo):** These drugs target a protein called PD-1 and improve T cells' ability to produce an immune response against cancer cells. In some countries, these drugs are only approved for treating esophageal cancer in patients whose tumors produce high levels of a protein called PD-L1. Ask your doctor if you are a candidate. These drugs may be combined with chemotherapy.
• **Ipilimumab (Yervoy):** This drug boosts the body's immune response by attaching to and inhibiting a protein called CTLA-4 that is found on T cells, freeing them to attack cancer cells. This drug is approved for patients with advanced or metastatic esophageal squamous cell carcinoma.

While these treatments have helped many patients, esophageal cancer remains a serious health threat around the globe, taking over 500,000 lives a year. Researchers in labs all over the world are working to find better therapies and possibly even a cure, with more than 300 clinical trials of new therapies for esophageal cancer currently underway or getting ready to recruit volunteer patients. Massive Bio is helping to raise awareness about esophageal cancer and other forms of the disease through our I Have Cancer campaign on social media. We can help patients with esophageal cancer find clinical trials of promising new therapies, too.



A CURE **FOR LONELINESS?**

New apps can help cancer patients make connections and feel less alone.

Living with cancer can be a lonely experience. Unfortunately, studies offer evidence for what many patients already know: Feeling isolated from others can make it harder to cope with cancer, both psychologically and physically. Loneliness goes hand in hand with stress, which is bad for overall health. Can technology, in the form of apps created to provide companionship and support, help people with cancer feel less lonesome?

It's hardly surprising that many cancer patients say they feel lonely. Symptoms and side effects of treatment can leave you feeling tired or just plain lousy, sapping you of any interest in socializing. Regrettably, some cancer patients find that certain friends or family members are reluctant to call or visit because they feel uncomfortable or don't know what to say. Older patients who have lost spouses or life partners may be most at risk for loneliness. In the United States, 27 percent of people over 60 live alone, according to the Pew Research Center. (Older people in most other countries are significantly more likely to live with extended family.)

Of course, you don't need to have a serious illness to be lonely—the United States is in the grip of an epidemic of loneliness, some

public health experts say, which was only worsened by the forced isolation brought on by the COVID-19 pandemic. A 2020 report by the National Academies of Sciences, Engineering, and Medicine found that more than one-third of adults aged 45 and older in the United States say they feel lonely, while nearly one quarter of adults aged 65 and older are socially isolated, meaning they have little contact with other people.

Increasingly, doctors and scientists have expressed concern about the potential health effects of loneliness. Humans are social creatures and hardwired for connection with others. We evolved to rely on family and friends for all kinds of support, including companionship, so isolation goes against our nature—and can make us sick. "Loneliness and weak social connections are associated with a reduction in lifespan similar to that caused by smoking 15 cigarettes a day and even greater than that associated with obesity," wrote U.S. Surgeon General Vivek Murthy wrote in the *Harvard Business Review*. Studies also indicate that people who experience social isolation have an increased risk of dementia, heart disease, stroke, heart failure, depression, anxiety, and suicide.

Loneliness and cancer

Several studies have shown that getting diagnosed with cancer can lead to loneliness. In a 2015 study published in the journal *Psycho-Oncology*, Dutch researchers gave a questionnaire that measures loneliness to three groups of subjects: elderly patients (aged 70 or older) recently diagnosed with cancer, younger cancer patients (50 to 69 years old), and older people without cancer. Interestingly, the older patients with cancer started out with lower levels of depression than their peers without cancer. A year later, researchers asked the three groups to fill out the questionnaires again. The older patients with cancer reported significantly increased levels of loneliness, as did the younger patients, to a somewhat lesser extent. Older people without cancer had no change.

Social isolation can continue even if you're cured, one study found: Young adult survivors of childhood cancer reported higher levels of loneliness than their peers who nev-

er had cancer. Too much alone time can be hard on the psyche for many patients. A 2022 study in the *International Journal of Environmental Research and Public Health* found that lung cancer patients who felt lonely much of the time were significantly more likely than others who didn't experience loneliness to become depressed. During the height of the COVID-19 pandemic, some cancer patients who felt isolated were 4.5 times more likely than others to become depressed.

Whether loneliness worsens cancer outcomes has not been well studied, though a 2021 study in *Psychiatry Research* found that Finnish men who reported lonely feelings were more likely than others to be diagnosed with cancer. However, during times of stress, lonely people produce higher levels of inflammation, one study found. Chronic inflammation can stoke some forms of cancer, as well as promote heart disease and other conditions. While some people cherish solitude and don't require frequent social contact, for many cancer patients taking steps to prevent loneliness can be good medicine.

Can apps help?
If you are struggling with loneliness, taking certain steps can help ease your angst. Joining a cancer support group, which may meet in person or by videoconference, will introduce you to people who understand what you're going through and can offer sympathetic ears. If a friend hasn't visited since you were diagnosed, break the ice with an invitation to drop by. Be honest with your loved ones and tell them you need their support and connection.

However, a new option for fighting loneliness has emerged in recent years. Several new "social health" companies now offer companionship and support—emotional and practical—for people who live alone or lack social contacts. Access to these services is typically offered through an app that can be downloaded from the App Store or Google Play. Some are only available through health insurance plans, while others charge a membership fee. Here are several of the most popular apps for overcoming loneliness.

Wisdo (wisdo.com): Wisdo has various "communities" that focus

on different topics, such as mental health, physical health, identity, family, and others. The app is designed to match users to others on the basis of their shared life experiences. The goal is to connect "buddies" who have dealt with the same issues. Wisdo users who prove to be most helpful (as rated by their peers) can become elevated to the status of guide. The app also has coaches who help users develop life skills. Wisdo conducted a survey and found that after three months of using the app, 58 percent of participants reported lower rates of loneliness. What's more, the number of users who had experienced severe loneliness was decreased by 19 percent, and 13 percent of participants were no longer lonely, according to a loneliness-screening test.

HearMe (www.hearme.app): HearMe's slogan is: "Be yourself. We'll listen." The HearMe app allows you to send a text that will be read by a specially trained person who will respond and offer emotional support. The app provides "a judgment-free space where you can discuss whatever is on your mind," according to the company website. HearMe collaborated with researchers from several major universities and a hospital in a study showing that users reported a 57 percent improvement in mood after a single conversation with one of the company's "listeners."

Papa (www.papa.com): Papa connects users to real people for companionship, as well as help with everyday tasks, transportation, and more. This service is available through Medicare Advantage and Medicaid, as well as some commercial health plans and corporate wellness programs.

Pyx Health: This service combines support from trained humans known as ANDYs (which stands for Authentic, Nurturing, Dependable, Your friend) and a chatbot called Pyxir. Members can make as many phone calls as they wish for companionship. ANDYs and Pyxir also provide support and help with finding and obtaining resources for users' physical, social, and mental health needs. Pyx Health is available through some commercial insurance plans.

KEEPING A COOLER HEAD

Can scalp-cooling caps help chemo patients hold on to their hair?

Photo courtesy of DigniCap

It's the side effect of chemotherapy that many patients dread the most: Hair loss. Up to 58 percent of female patients who require chemotherapy call the threat of losing hair the most disturbing aspect of the treatment, according to one study, while another 8 percent of patients are so concerned about the risk of going bald that they consider refusing chemo altogether.

Can chilling out help chemotherapy patients avoid shedding their locks? Scalp cooling to preserve hair during chemo treatment is an idea that originated in Europe in the 1970s. Techniques for chilling the scalp have become significantly more sophisticated since then, however. And skepticism about the practice has largely been replaced by acceptance, as research suggests that scalp cooling can help a significant portion of patients preserve at least some of their hair.

From ice packs to cold caps

Doctors use the term alopecia (al-oh-PEE-shuh) to refer to the partial or total loss of hair where it should normally grow. Alopecia caused by chemotherapy occurs most commonly on the scalp, especially on the crown and sides of the head. Not all patients who are treated with chemotherapy lose hair, and the risk of alopecia depends on which drug or drugs you receive. When hair loss does occur, it usually begins a week or two after treatment begins. Once treatment ends, hair grows back after three to six months. By one estimate, about two-thirds of patients' hair undergoes a change in color or texture: A brunette may turn gray, for example, or once-curly locks may straighten, and vice versa. These changes are often temporary, though. No one is sure how scalp cooling (also called scalp hypothermia) preserves hair, but one theory is that cold temperature causes blood vessels in the scalp to constrict, or become narrow. That prevents chemo drugs, which travel in the blood, from reaching hair follicles and harming cells that make each strand grow. The deep freeze might also slow down the metabolic activity of cells in hair follicles, making them less vulnerable to

the effects of chemo, which tends to attack rapidly dividing cells.

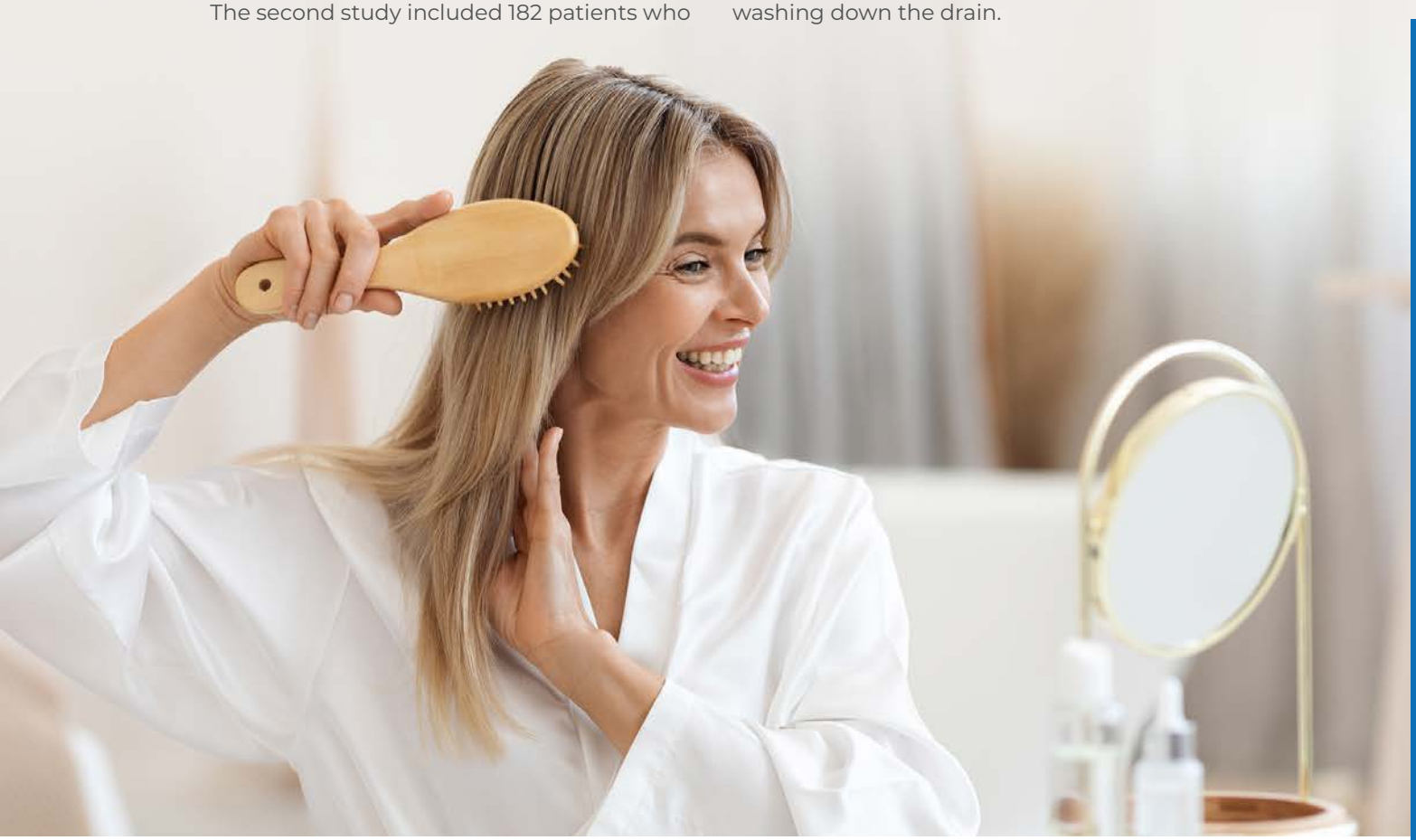
In the past, patients chilled their scalps with packs of ice, but many now use devices known as cold caps or cooling caps. Several are approved by the U.S. Food and Drug Administration (FDA), including devices made by Cooler Heads, DigniCap, and Paxman. While receiving chemotherapy, the patient wears headgear that resembles a helmet and is connected by a tube to a cooling system that circulates cold liquid through the device, which produces a chilling effect on the scalp.

Backed by research

In the past, many doctors had doubts about the benefits of scalp cooling, but two studies published in *JAMA* in 2017 have helped to eliminate much of that skepticism, at least with regard to FDA-approved devices. In one, 101 patients with early-stage breast cancer who were undergoing chemotherapy used the DigniCap device. They were compared with 16 similar patients who didn't use the device and served as a control group. In the group that received scalp cooling, 66.3 percent of the patients achieved the threshold for success, which was less than 50 percent hair loss; no one in the control group met that threshold. What's more, DigniCap users reported feeling less bothered by hair loss and better about their appearance.

The second study included 182 patients who were undergoing various chemotherapy regimens for breast cancer. Two-thirds used the Paxman device, while the remainder did not receive scalp cooling. A doctor who was unaware which group patients were in judged whether hair preservation was successful, which was defined as loss of less than 50 percent of hair. Overall, scalp cooling was effective in 50.5 percent of users, while none of the patients in the control group had significant hair preservation. However, this study and others have found that scalp cooling is somewhat less effective at saving hair in patients receiving anthracycline-based chemotherapy than in those undergoing other regimens.

Some doctors have expressed concern that keeping chemotherapy away from hair follicles by reducing the flow of blood could promote metastases, or the spread of cancer, to the scalp. However, studies have failed to find any evidence that's true. The most-documented downside to scalp cooling is that many patients find it uncomfortable—enough so that some decide it's not worth it and give up. Patients have compared the sensation that cold caps induce to the gnawing brain pain that can happen when you eat or drink something very cold, often called an "ice cream headache." But users say the unpleasant feeling eventually eases, and many insist it's worth tolerating for the possibility of keeping some or all of your mane from washing down the drain.



PATIENT ADVOCACY

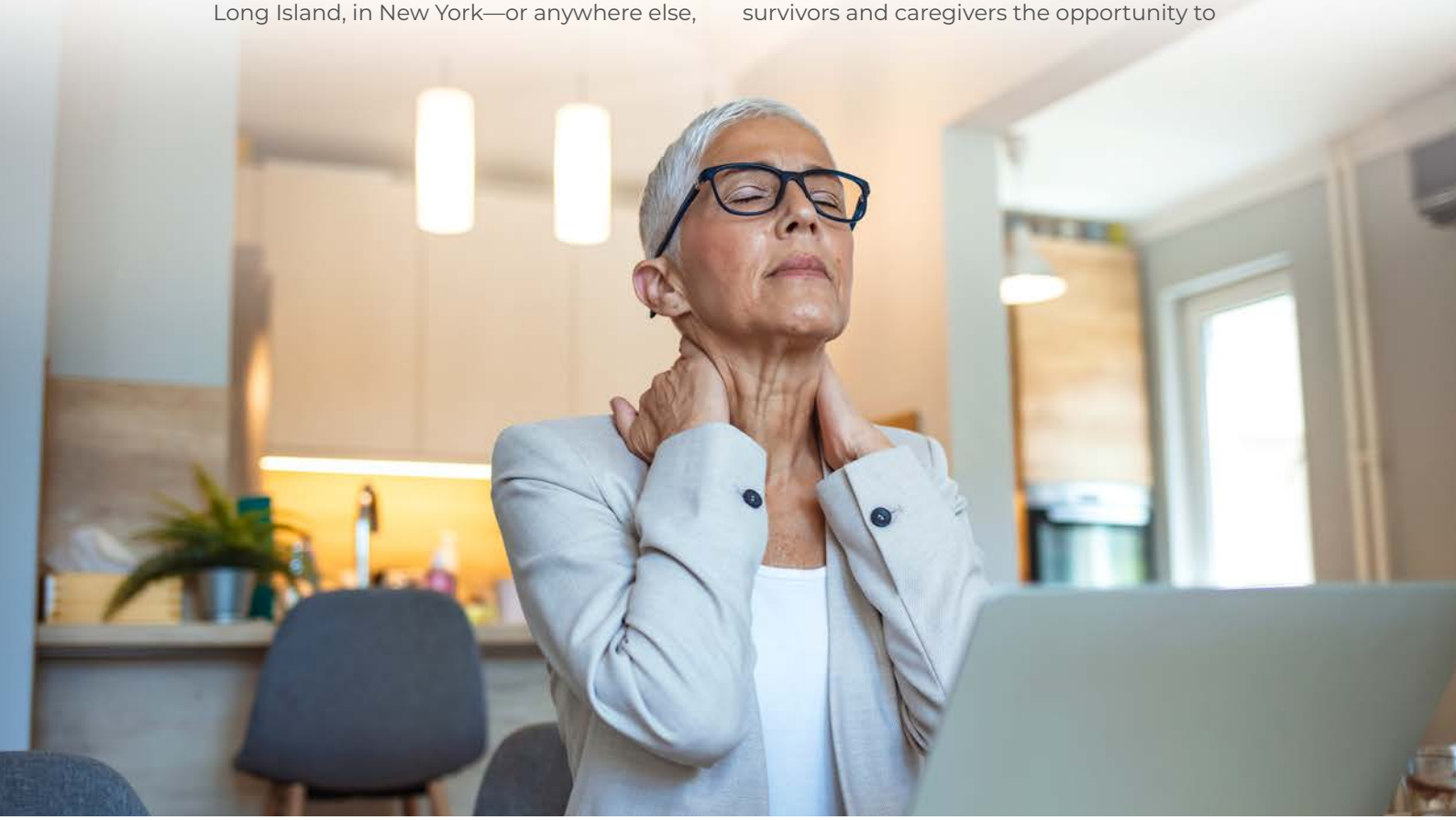
SPOHNC

Patients with head and neck cancers face unique challenges, but SPOHNC provides emotional support, information, and hope.

During a routine checkup in 1990, Nancy Leupold's dentist noticed a suspicious lesion, or sore, in her mouth. The dentist referred Leupold to an oral surgeon, who diagnosed squamous cell carcinoma, a form of oral cancer. Squamous cell carcinomas that affect the mouth, throat, voice box, sinuses, and salivary glands are often grouped together and are known collectively as head and neck cancers. Head and neck cancer is the sixth most common form of cancer worldwide, with close to 900,000 new cases and about 450,000 deaths per year—and its incidence is rising in many parts of the globe.

Leupold was frightened by the diagnosis, but soon became frustrated when she was unable to find a support group for people with head and neck cancers near her home on Long Island, in New York—or anywhere else, for that matter. Her family and friends were sympathetic about the challenges she faced, but they couldn't truly understand what she was going through as a person living with a form of head and neck cancer. When she told her surgeon about her inability to find a support group of like-minded and empathic patients, his response surprised her: Why don't you start one?

Leupold did just that in 1991, forming Support for People with Oral, Head and Neck Cancer (SPOHNC), the first group of its kind in the United States. There were nine people, including Leupold, at the new organization's first meeting. Today, there are over 100 SPOHNC (pronounced "spunk") chapter support groups across the country that meet regularly, giving newly diagnosed patients, survivors and caregivers the opportunity to



talk and listen to others who know what it's like to live with head and neck cancers.

"They come to be with others who have traveled a similar journey," says SPOHNC's executive director, Mary Ann Caputo, who notes that people with head and neck cancer often live with unique and sometimes difficult circumstances. The disease and its treatment can leave patients with long-term or permanent changes that may be psychologically and socially challenging, such as facial disfigurement, difficulty swallowing, dry mouth, sores in the lining of the mouth and throat, and others. "For some patients, it becomes very debilitating," says Caputo.

"These people feel very isolated and alone," adds SPOHNC's outreach administrator, Chris Leonardis. "They need to talk to people who understand. And that's why we're here."

SPOHNC unites people with head and neck cancer through its support groups, as well as a private Facebook page for patients and survivors, where members can share their questions, concerns, and offer support. However, support is also available on a one-to-one basis by way of SPOHNC's National Survivor Volunteer Network, which was introduced in 2004. This matching service brings together volunteers who have survived head and neck cancer with patients who are newly diagnosed or who are currently undergoing or recovering from treatment. Caregivers can be matched, too. SPOHNC's website emphasizes that these pairings allow patients and their loved ones who are coming to grips with a cancer diagnosis to share the experience with "someone who has walked in their shoes."

Caputo recalls one match that sums up what the Survivor Network does for these patients—and for the volunteers themselves. "There was a patient who was treated many, many years ago, but who still had swallowing and dry mouth challenges," says Caputo. "She was at her wits' end because her family and friends did not believe her." The woman's symptoms were so severe that her weight had plummeted and she even contemplated taking her own life. SPOHNC was able to connect her with a volunteer who listened and assured her that she wasn't crazy. He encouraged her to see a specialist for swallow therapy and try a feeding tube to regain some weight, if necessary. Later, the volunteer thanked SPOHNC for allowing him to connect with the woman. "I am so happy that I am volunteer," he said. "I think I actually saved a life today."

In addition to providing emotional support,

an important aspect of SPOHNC's mission is to educate patients about their cancers, which it does in a variety of ways. SPOHNC's website features an FAQ section about head and neck cancers that explains critical information in plain language, such as what type of side effects patients might expect from treatment. The organization also holds webinars led by top physicians and other healthcare professionals in the field of head and neck cancer that allow patients to learn more about their conditions, treatment options, and side effects they may experience.

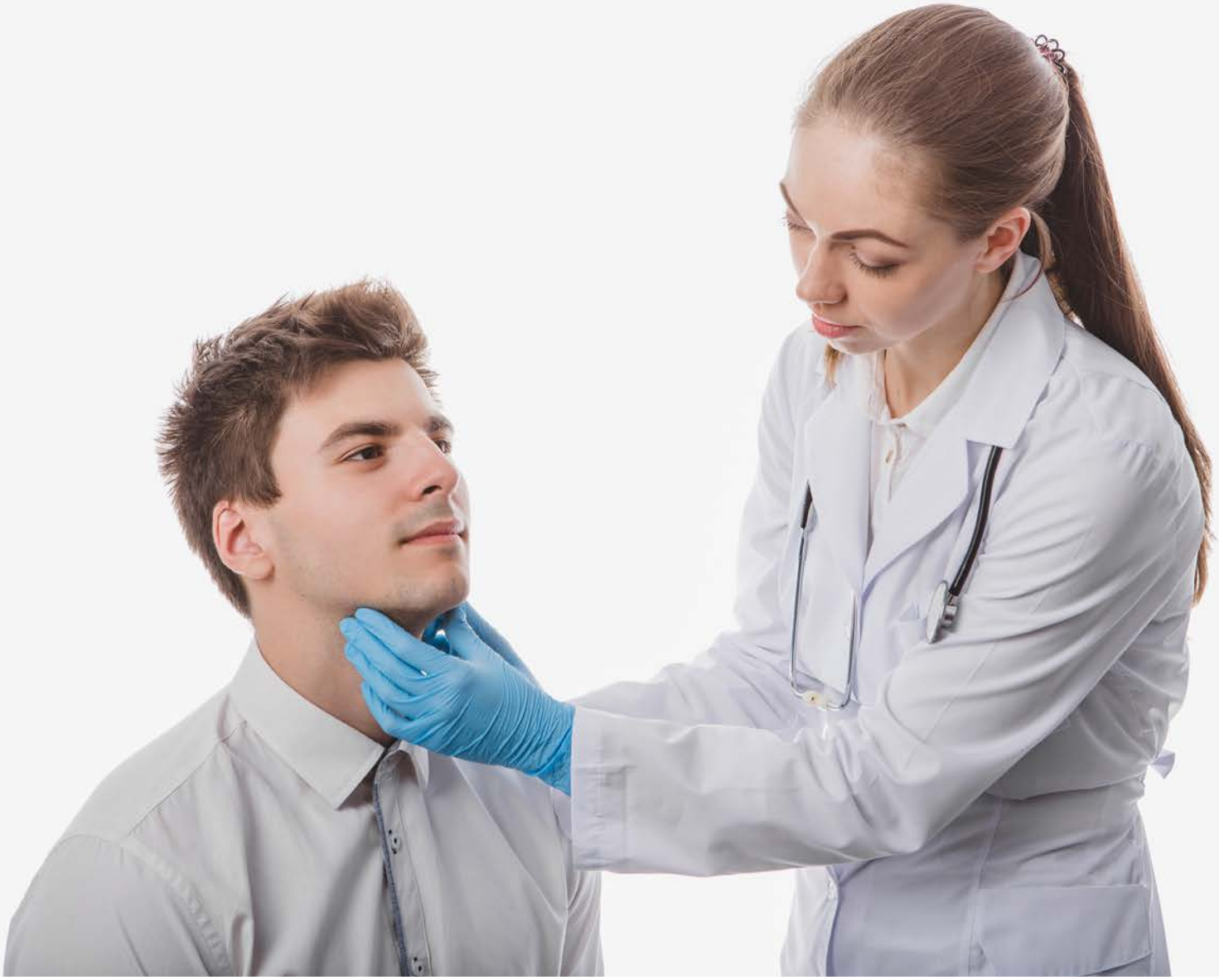
What's more, SPOHNC publishes several popular books, including *We Have Walked in Your Shoes: A Guide to Living with Oral, Head, and Neck,* for newly diagnosed patients, as well as two volumes of *Eat Well Stay Nourished: A Recipe and Resource Guide for Coping with Eating Challenges.* The organization also produces a monthly newsletter, edited by Leonardis, that features a variety of content, such as stories about new treatments and how to cope with treatment side effects. Practical topics are covered, too, such as how to maintain a healthy diet—a critical issue for all cancer patients, but especially for many patients with head and neck cancers. Other recent articles covered topics such as how to discuss a cancer diagnosis with your children and current lobbying efforts to enact legislation that would expand Medicare coverage of dental services. The newsletter also includes stories shared by survivors about their experience coping and living with cancer.

Along with providing patients tools to better understand and manage their malignancies, SPOHNC also places a great emphasis on helping people with head and neck cancers recognize the importance of clinical trials. "Many people are afraid or they don't know

how to find a clinical trial," says Caputo. The National Library of Medicine lists all clinical trials of new cancer therapies on the website clinicaltrials.gov, "but it's massive and confusing," says Caputo, which is why SPOHNC's website features extensive information about what clinical trials are, how they work, and how to find one. That includes offering a link that allows users to contact Massive Bio to learn about their treatment options beyond standard of care and currently approved therapies.

April is Oral, Head and Neck Cancer Awareness Month, which SPOHNC will recognize in various ways, such as sharing stories of their volunteers and survivorship in its newsletter and on social media. Some chapters are holding oral cancer screenings, walk-a-thons, and other events. More than a dozen historic buildings, bridges, natural wonders, and other structures across the country will be illuminated in burgundy and white to raise awareness about head and neck cancers.

SPOHNC Founder Nancy Leupold died in 2020, after living for three decades as a survivor of head and neck cancer, while helping to make life more satisfying and fulfilling for others like her. That mission continues through the work of Caputo, Leonardis, and their colleagues and volunteers at SPOHNC. "The more we have to offer patients and survivors and their families, the better off they'll be," says Caputo. "This was Nancy's vision and we want to keep her legacy alive."



Awareness Calendar

April

- Esophageal Cancer Awareness Month
- Head and Neck Cancer Awareness Month
- National Cancer Control Month
- National Minority Cancer Awareness Month
- Testicular Cancer Awareness Month
- World Health Day (April 7)

May

- Bladder Cancer Awareness Month
- Brain Cancer Awareness Month
- Melanoma and Skin Cancer Awareness Month
- National Cancer Research Month

June

- Cancer Immunotherapy Awareness Month
- National Cancer Survivors Month

July

- Sarcoma and Bone Cancer Awareness Month
- Ultraviolet (UV) Safety Awareness Month

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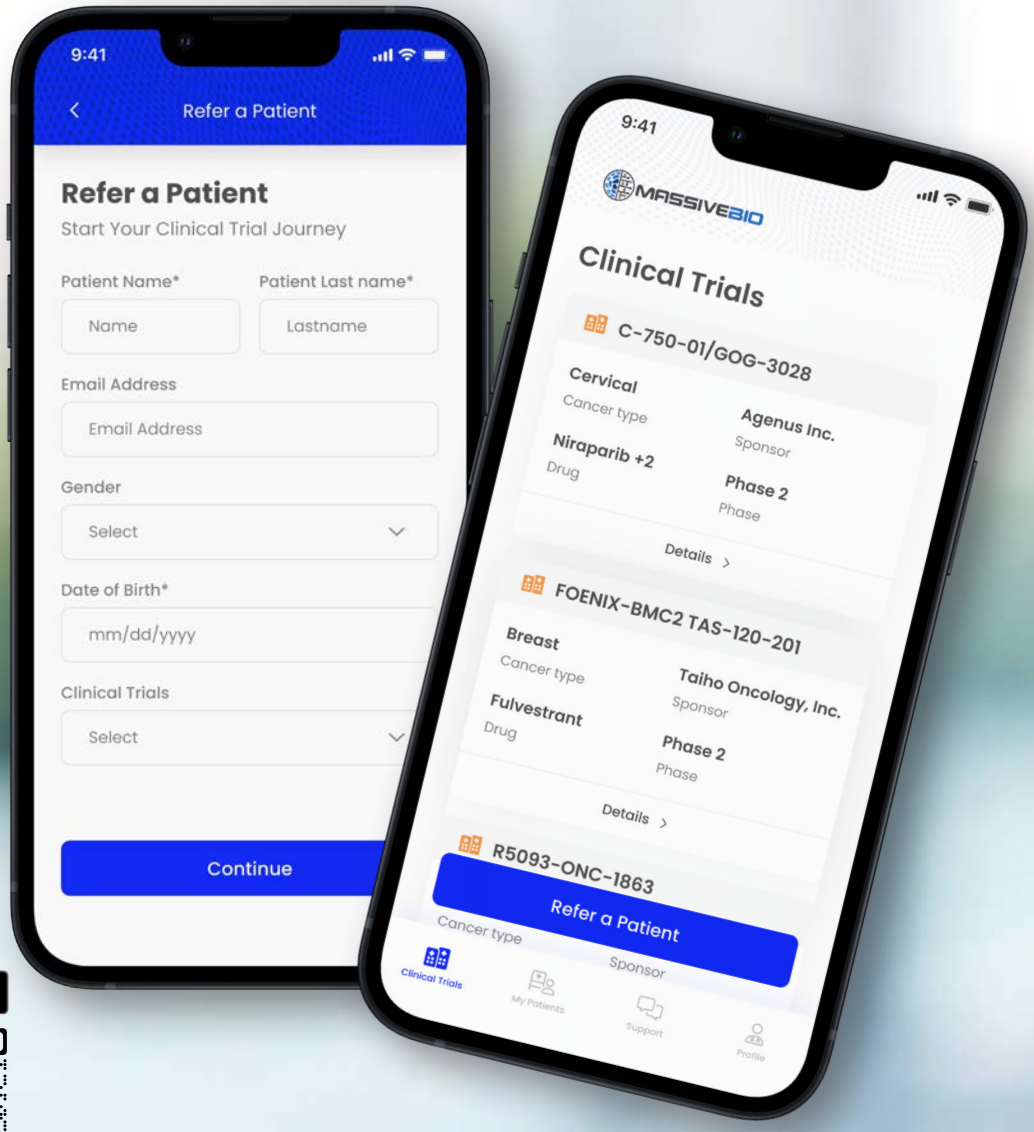

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SYNERGY-AI Cancer Clinical Trial Finder is a mobile app that uses your cancer type, stage, biomarker status, and other data points to identify clinical trials of cutting-edge treatments, at research sites near you. Contact us about enrolling in a clinical trial and let Massive Bio do the rest.