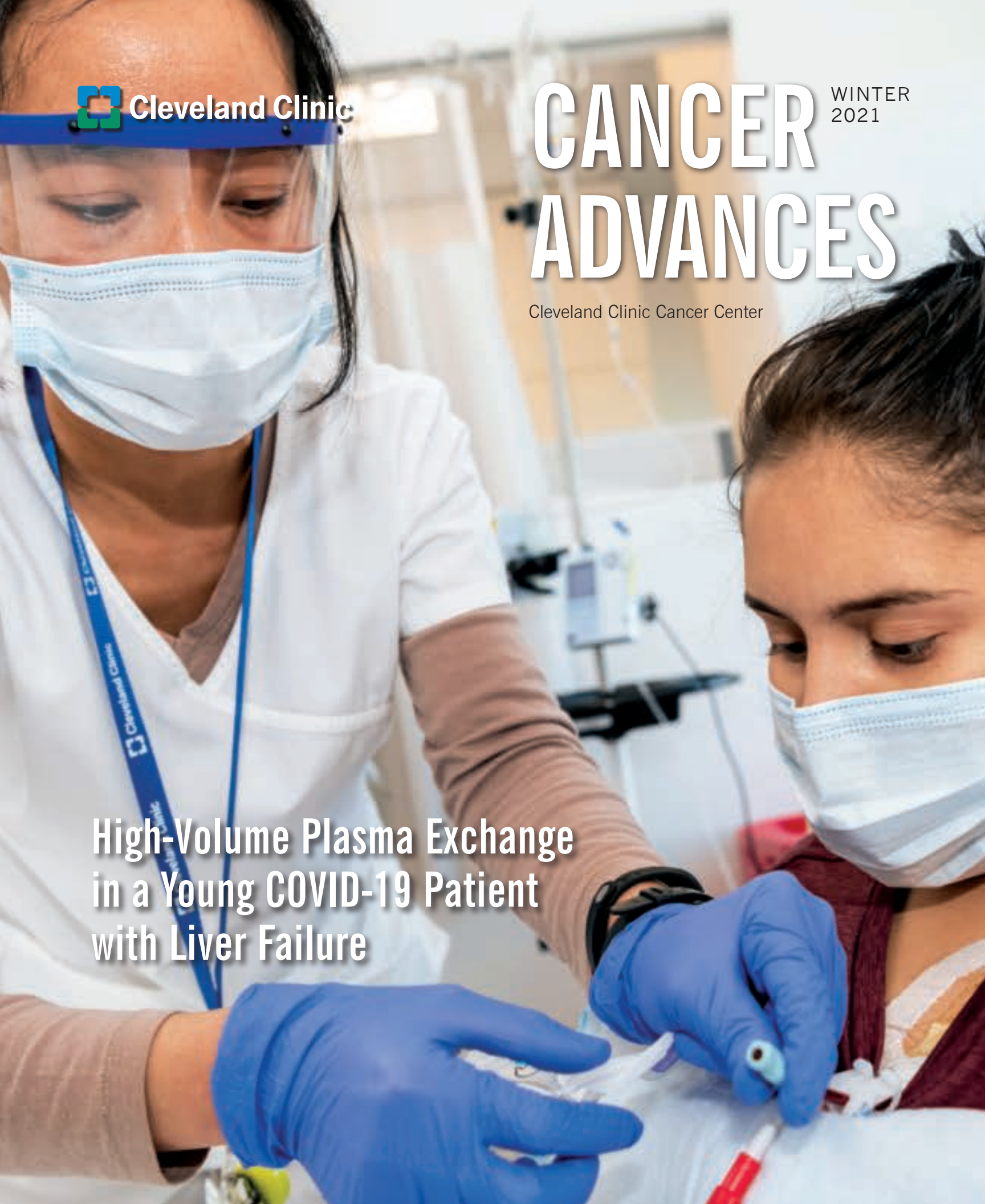


Cleveland Clinic

# CANCER ADVANCES

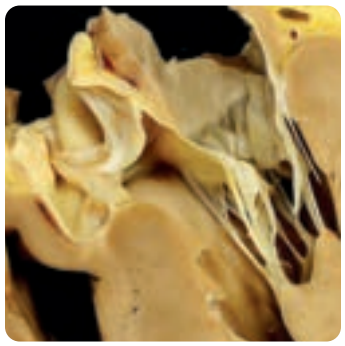
WINTER 2021

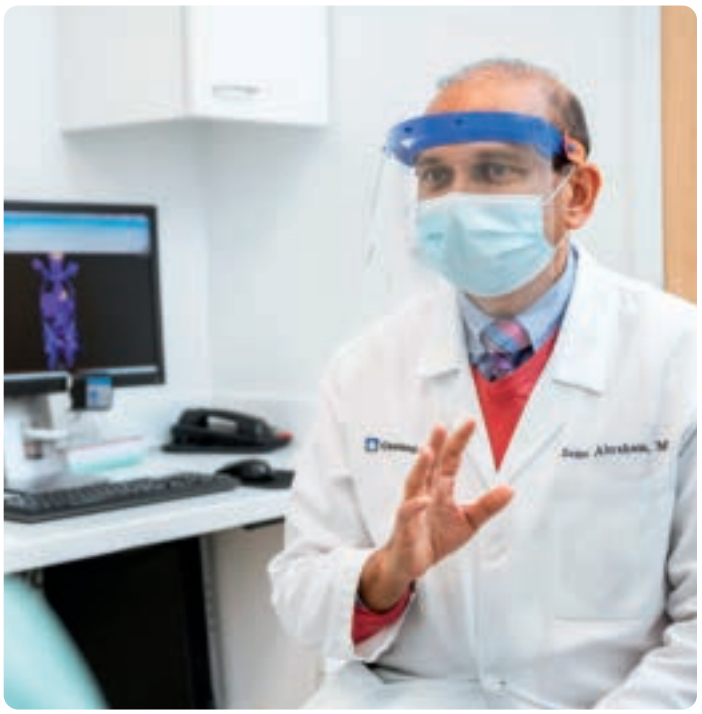
Cleveland Clinic Cancer Center

## High-Volume Plasma Exchange in a Young COVID-19 Patient with Liver Failure

Cleveland Clinic Cancer Center provides complete cancer care enhanced by innovative basic, genetic and translational research. It offers the most effective techniques to achieve long-term survival and improve patients' quality of life. The Cancer Center's more than 700 physicians, researchers, nurses and technicians care for thousands of patients each year and provide access to a wide range of clinical trials. Cleveland Clinic Cancer Center unites clinicians and researchers based in Taussig Cancer Institute and in Cleveland Clinic's 26 other clinical and special-expertise institutes, as well as cancer specialists at our regional hospitals, health centers, Cleveland Clinic Florida and Cleveland Clinic Abu Dhabi. Cleveland Clinic is a nonprofit academic medical center ranked as a top hospital in the country *(U.S. News & World Report)*, where more than 4,500 staff physicians and researchers in 180 specialties collaborate to give every patient the best outcome and experience.

# INSIDE





# DEAR COLLEAGUES,

BRIAN J. BOLWELL, MD, FACP
Chairman, Taussig Cancer Institute
Cleveland Clinic Cancer Center
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On Twitter: @BrianBolwellMD

Welcome to the latest edition of *Cancer Advances*. This year marks 100 years of innovation in medicine, research and education at Cleveland Clinic, and I am proud that this issue of *Cancer Advances* demonstrates our continued leadership in these areas.

The programs and projects described in this issue reflect Cleveland Clinic Cancer Center's emphasis on high-impact, translational cancer research and innovative therapies. The work highlighted here is the result of dozens of talented clinicians and researchers working together to advance patient care in the midst of a global pandemic that has changed cancer care for the foreseeable future (p. 10).

Our cover story offers a glimpse into how innovative therapies can benefit the sickest patients, like the young woman with COVID-19 and liver failure saved by advances in transfusion medicine (p. 4) or the "clean sweep" surgical procedure that saved a woman's remaining small bowel (p. 22). We also highlight our leadership in a global trial of a new drug for patients with breast cancer (p. 8) and of a blood test that could revolutionize cancer screening (p. 14).

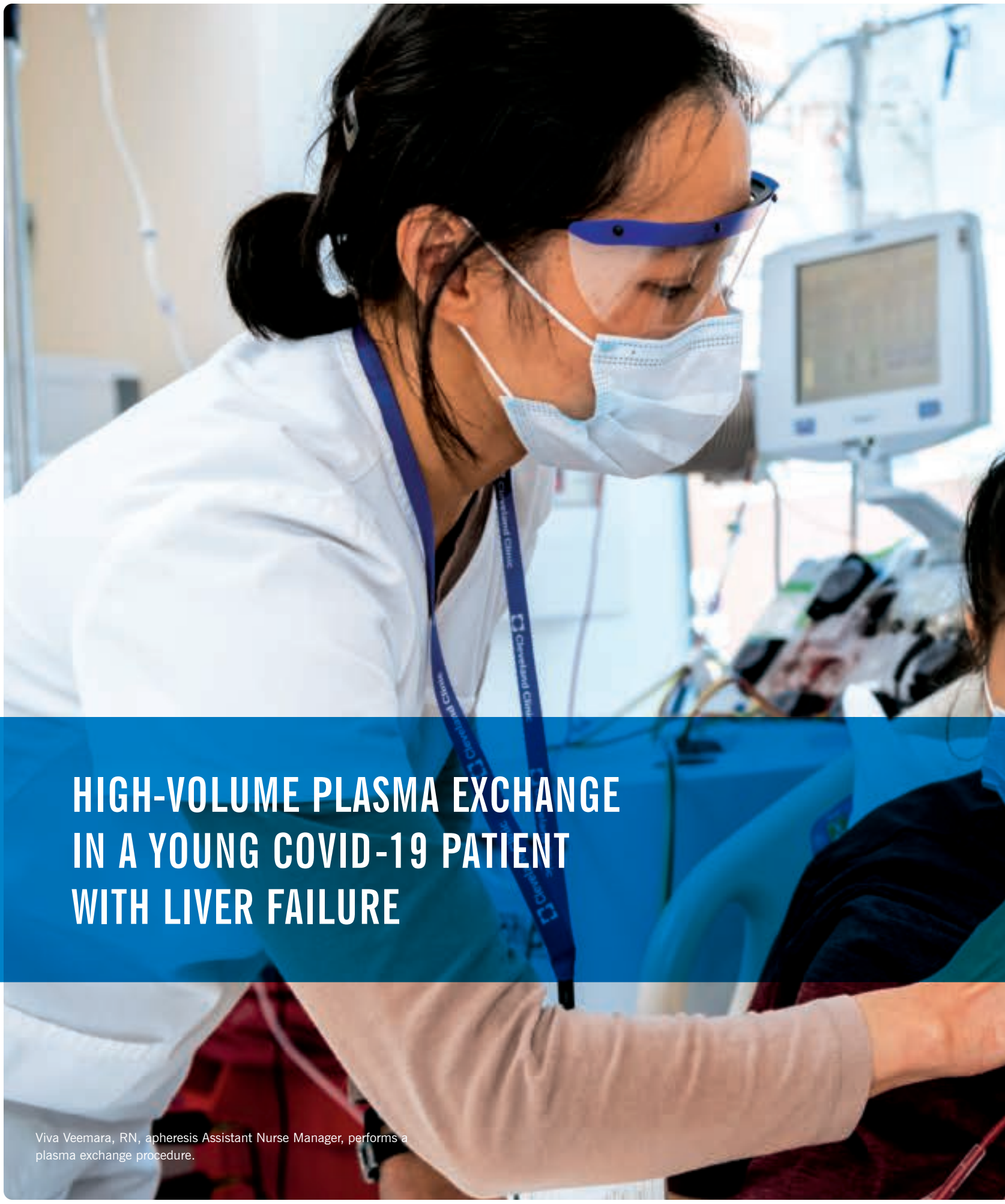
Our expertise in rare cancers and blood disorders such as systemic light-chain amyloidosis (p. 12) and central nervous system lymphoma (p. 20) remains a strong and growing focus as we seek to expand our reach to offer care to even the most challenging cases and patients.

Funds raised in this year's Virtual VeloSano will be allocated to projects that promise to offer meaningful innovations for our patients. While the pandemic may have changed the format of VeloSano this year, it has not changed its mission: to pursue a "swift cure" for cancers from common to rare.

As always, I welcome the opportunity to discuss the research projects and treatment initiatives underway at Cleveland Clinic Cancer Center and the possibilities for collaboration. Don't hesitate to reach out with ideas, questions, concerns or suggestions.

Sincerely,

Brian J. Bolwell, MD, FACP
Chairman, Taussig Cancer Institute
Cleveland Clinic Cancer Center



# HIGH-VOLUME PLASMA EXCHANGE IN A YOUNG COVID-19 PATIENT WITH LIVER FAILURE

Viva Veemara, RN, apheresis Assistant Nurse Manager, performs a plasma exchange procedure.

# HIGH-VOLUME PLASMA EXCHANGE IN A YOUNG COVID-19 PATIENT WITH LIVER FAILURE

*Bridge to transplant after acetaminophen overdose*

**KEY POINTS**

Apheresis was successfully used as a bridge to transplant in a patient suffering from acetaminophen overdose after COVID-19 diagnosis.

High-volume plasma exchange treats a patient's plasma three to four times.

This patient was the first at Cleveland Clinic treated with this approach.

The patient had an uneventful recovery and is doing well.

In June 2020, a 27-year-old woman developed a case of COVID-19; her main symptoms were stomach pain, nausea and diarrhea. To relieve the pain, she took so much acetaminophen that she had an overdose and developed fulminant hepatic failure.

She was gravely ill and hospitalized at Cleveland Clinic in the COVID-19 ICU. She was intubated and treated for symptoms of liver failure, which included cerebral edema.

To normalize her blood pressure, she was treated with high-dose vasopressors. The liver failure also caused a cytokine storm, which stressed her heart and kidneys. She was in need of a liver transplant but was considered too high risk. "Every moment, she was getting worse and further from being able to get a liver transplant," says Kristin Ricci, MD, a transfusion medicine specialist and Medical Director of the apheresis unit at Cleveland Clinic.

## High-volume plasma exchange administered

Cleveland Clinic is one of only a few medical centers worldwide able to perform high-volume plasma exchange. During the procedure, a patient's plasma is removed with an apheresis instrument and is replaced with plasma from healthy donors. Unlike standard plasma exchange treatments, which treat a patient's plasma once, high-volume plasma exchange treats it three to four times. This patient was the first at Cleveland Clinic treated with this approach; the goal was to stabilize her health so she could get a transplant.

The procedure was a team effort involving the intensive care, hepatology, anesthesiology, liver transplant, nursing, apheresis, laboratory medicine and blood bank teams. "High-volume plasma exchange requires great resources and coordination. Many different groups used their strengths to save this patient's life — Cleveland Clinic culture at its best," says Dr. Ricci.

After the procedure, the patient became more hemodynamically stable, her vasopressor requirements decreased and many of her liver labs normalized. The procedure also removes inflammatory cytokines, so the storm subsided. Because of these major improvements, the patient was listed for a liver transplant.

The liver transplant team, led by Giuseppe D'Amico, MD, and Jacek Cywinski, MD, was ready to perform the transplant. The next day, the patient received a second high-volume plasma exchange and showed continued improvement in clinical status and labs. The transplant was performed that evening by a team that included more than 40 caregivers.

## A life transformed

The patient had an uneventful recovery and has been discharged home and is doing well. "The high-volume plasma exchange was a game changer that saved her life. This technique completely changed the management strategy for this patient. We are excited about starting a program to use high-volume plasma exchange for

Cleveland Clinic is one of only a few medical centers worldwide able to perform high-volume plasma exchange.

LEFT: Viva Veemara, RN, performs a plasma exchange procedure.

acute liver failure," says Cristiano Quintini, MD, Program Director and Surgical Director of the Liver Transplantation Program.

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*Dr. Ricci directs Cleveland Clinic's apheresis unit. She can be reached at riccik2@ccf.org or 216.444.2633.*

*Dr. D'Amico is a transplant surgeon. He can be reached at damicog@ccf.org or 216.445.3388.*

*Dr. Cywinski is Quality Review Officer in the Department of General Anesthesiology. He can be reached at cywinsj@ccf.org or 216.444.2305.*

*Dr. Quintini directs the Liver Transplant Program. He can be reached at quintic@ccf.org or 216.445.3388. On Twitter: @CrisQuintiniMD*

# GLOBAL TRIAL SEEKS NEW GOLD STANDARD TREATMENT FOR HER2+ EARLY BREAST CANCER IN POST-NEOADJUVANT SETTING

*New drug among the most potent antibody-drug conjugates in development*

**KEY POINTS**

A global phase 3 clinical trial will investigate a novel drug in the post-neoadjuvant setting for HER2+ breast cancer patients.

This trial examines trastuzumab deruxtecan (T-DXd) versus trastuzumab emtansine (T-DM1).

Some 1,600 patients will be enrolled in this trial, led by Jame Abraham, MD, Chair of Cleveland Clinic Cancer Center's Department of Hematology and Medical Oncology.

HER2+ breast cancers are among the most aggressive forms of breast cancer, with an increased chance of recurrence and relapse and decreased overall survival. Now a new global phase 3 clinical trial will investigate a novel drug in the post-neoadjuvant setting that researchers hope will be a significant improvement over the current standard of care.

Around 15% to 20% of breast cancer patients have HER2 overexpression. In the KATHERINE trial, T-DM1 (trastuzumab emtansine), substantially improved disease-free survival for patients who had residual disease after neoadjuvant taxane-based chemotherapy and HER2-targeted agents (trastuzumab +/- pertuzumab).

"This was great news for many patients, but a subset of high-risk patients maintain a high chance of relapse," says Jame Abraham, MD, Chair of the Department of Hematology and Medical Oncology at Cleveland Clinic Cancer Center, who is leading the trial. "The current trial is looking at trastuzumab deruxtecan [T-DXd; DS-8201a] versus T-DM1 in the post-neoadjuvant setting for patients with residual disease and at a higher risk of recurrence."

This trial (NSABP B 60/DESTINY-Breast 05) will enroll HER2+ patients who were treated with taxane-based chemotherapy and trastuzumab (+/- pertuzumab), had residual disease after surgery, and are at high risk of recurrence, which includes patients with large, inoperable tumors at presentation or who are node positive after preoperative therapy. Patients will be randomized to either T-DXd every three weeks for 14 cycles or T-DM1 every three weeks for 14 cycles. The primary endpoint is invasive disease-free survival.

"The question is: Can we do better than T-DM1 in these high-risk patients?" says Dr. Abraham.

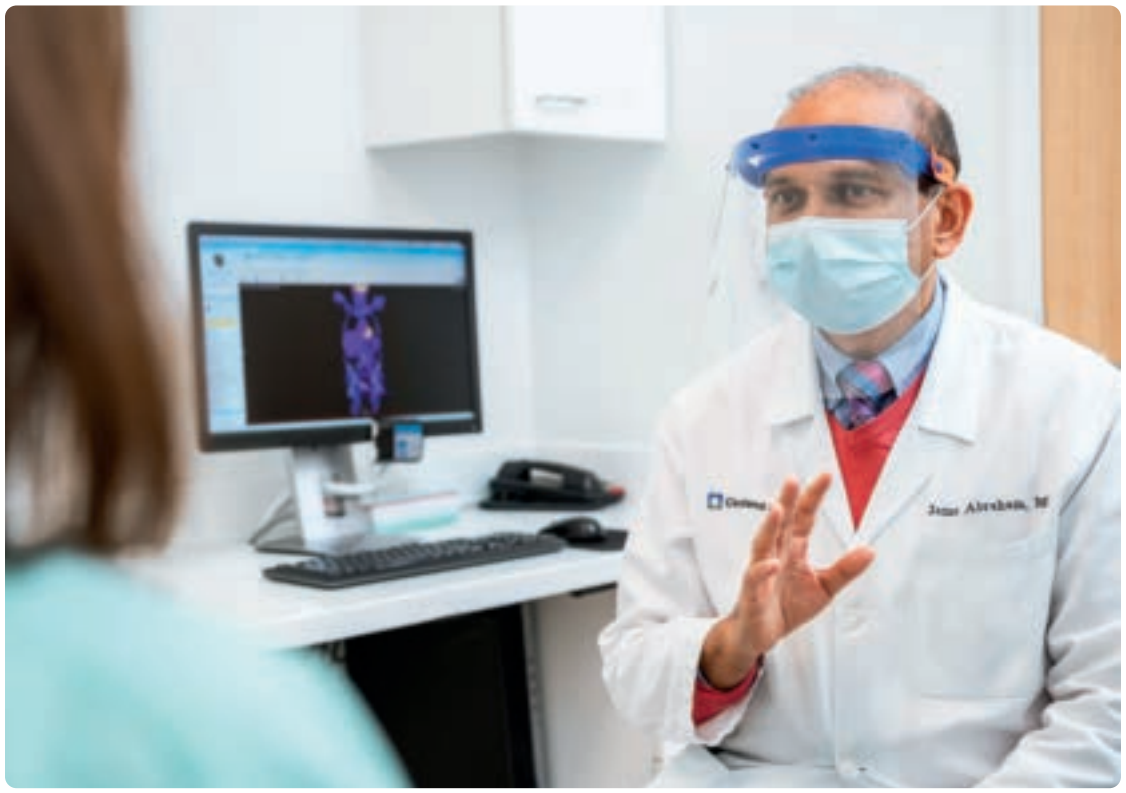
## More powerful, with a shorter half-life

Both medications are antibody-drug conjugates, but T-DXd is highly potent, with a drug-to-antibody ratio of 8. Its payload also has a shorter half-life, reducing systemic exposure, and is membrane permeable, which allows for elimination of both HER2-targeted tumor cells as well as surrounding tumor cells. It features a tumor-selective cleavable linker.

"It's probably one of the most active antibody-drug conjugates in development," Dr. Abraham says.

A phase 2 trial of T-DXd found significant response in HER2+ metastatic breast cancer patients who had previously been treated with T-DM1, with an objective response rate of 60.9% and median progression-free survival of 16.4 months.

One of the potential side effects identified in previous trials is an increased risk of interstitial



LEFT: Dr. Abraham speaks with a breast cancer patient.

lung disease (ILD), which is exacerbated further in patients who have received radiation. “That is a concern, and we need to make sure that we’re able to manage ILD and that patients don’t have too high a risk of developing it,” he says. “A robust monitoring and management plan is in place.”

Some 1,600 patients will be enrolled in this new global trial, which involves as many as 400 sites across 31 countries. The study will last approximately seven years.

*Dr. Abraham is Chair of the Department of Hematology and Medical Oncology. He can be reached at abrahaj5@ccf.org or 216.445.0150. On Twitter: @jamecancerdoc*

# BEYOND SOCIAL DISTANCING: CANCER CARE IN THE AGE OF COVID-19

*Psychosocial and downstream effects*

**KEY POINTS**

COVID-19 has accelerated the rate of adoption of telemedicine, and the changes are here to stay.

Experts fear a sharp increase in overall diagnoses, advanced diagnoses and cancer deaths in the coming months and years.

Delays in screening and treatment combined with economic consequences of the pandemic will widen existing disparities in cancer care.

Cancer patients have heightened fear and anxiety and fewer ways to cope with them due to the pandemic.

Cancer care is not exempt from the truism that COVID-19 has changed our world in unprecedented ways. Beyond the sheer logistics of keeping a cancer center safe for patients during a global pandemic lie the downstream effects of necessary safety measures, from the acceleration of telemedicine adoption to increased fear and anxiety. Matt Kalaycio, MD, Vice Chairman of Cleveland Clinic's Taussig Cancer Institute, discusses several ways that COVID-19 has changed the present and future of cancer care.

## The acceleration of virtual options for patient interactions

"One of the things I think will eventually be seen as a net positive is the way the pandemic has hastened the arrival of virtual medicine in both urban and rural locations. It has made us get comfortable with this technology quickly," says Dr. Kalaycio. "There is no substitute for the physical exam in medicine, but when reality demands that the risk of physical contact is too high, what's the best way to use these technologies? How can we expand our reach beyond our historically limited sense of geography?"

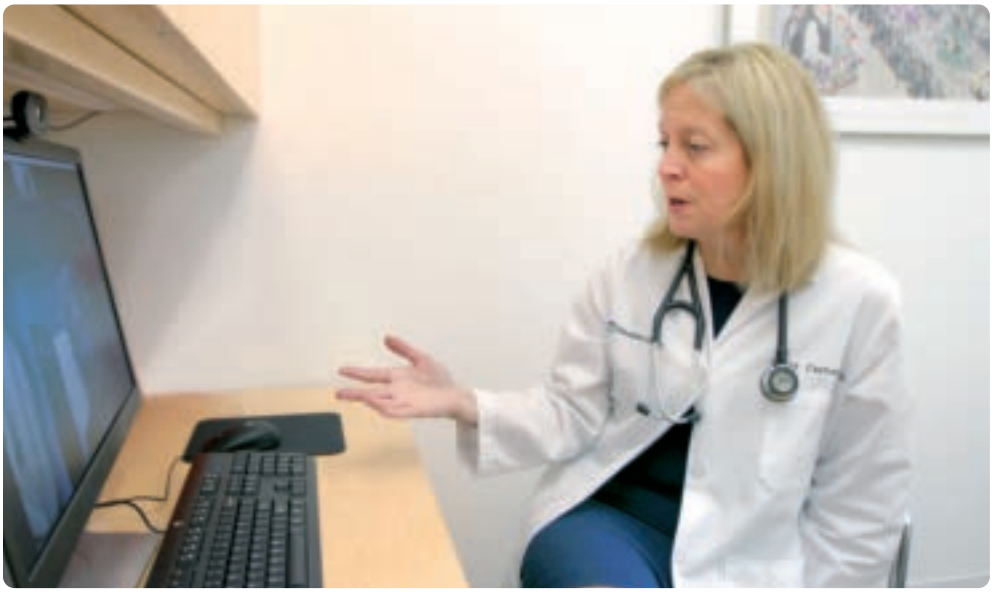
Cleveland Clinic patients without active cancer have the option to access routine follow-up care via telemedicine, or to delay in-person visits until a safer time. "We have even converted some visits for patients with active disease to telehealth," he notes. "They'll still need to come in for testing, infusions and the like, but we are reducing traffic in ways that don't negatively impact a patient's care."

Patients also need reassurance that seeking in-person care is safe. Cleveland Clinic is taking a comprehensive approach to ensure that cancer patients receive necessary care in the safest way possible, including adapting spaces for social distancing, using appropriate personal protective equipment, mandating masks in the building and screening all caregivers. "We have to reassure our patients that it's safe for them to come and get treatment here, and that staying at home can create a bigger problem."

## A potential surge in severity

Fear of contracting COVID-19 may lead to a potential surge of cancer cases diagnosed at later stages when there may be fewer treatment options, or of patients under surveillance who missed follow-up and thus may miss signs of recurrence.

"So many people have postponed seeing their doctors or getting routine screening done. They're ignoring symptoms that would have caused them to visit the doctor in our pre-pandemic world. Eventually, we're going to see all these patients," says Dr. Kalaycio. "Diagnosing cancer as early as possible is important in almost every type of cancer; so many people will have fewer treatment options and will be diagnosed later



LEFT: Hetty Carraway, MD, Leukemia Program Chair, conducts a virtual visit with a leukemia patient.

because of COVID-19." Experts fear a sharp increase in overall diagnoses, advanced diagnoses and cancer deaths in the coming months and years.

## Widening disparities

Delays in screening and treatment combined with economic consequences of the pandemic will widen existing disparities in cancer care. "This is my biggest concern. Even if we get a vaccine quickly, the economic effects will be sustained. Our most vulnerable populations will have financial insecurity, causing patients to delay or decline treatment," notes Dr. Kalaycio.

Cleveland Clinic's efforts to address disparities in healthcare delivery have accelerated during the pandemic. A collaboration with local religious organizations and the Langston Hughes Center has brought cancer screening to patients who might face barriers at a larger facility. "This has been especially important during the pandemic," says Dr. Kalaycio. "Many of these patients who are at greater risk of COVID-19 can avoid the higher-traffic hospital facilities and still get world-class cancer screening."

## Increased fear and uncertainty

Cancer patients already experience a high level of fear of the unknown. Add to the normal cancer worries the possibility of catching COVID-19, and fear and anxiety heighten even further.

"Patients aren't just scared of their cancer. They're scared to leave the house and catch something that might kill them," says Dr. Kalaycio. "And the many resources Cleveland Clinic has in place to mitigate this fear and anxiety they're not accessing because they're not visiting the clinic in person, and it takes time to make our social support programs virtual."

A common coping method for patients with cancer is the support of loved ones and family. Social distancing has made accessing that support even tougher. "I recommend patients call or video chat with friends and family regularly," he says, "but there's no question that this time has been tough on our patients."

Another way to mitigate fear of the unknown is planning. Determining alternative caregivers, food sources and transportation may allow patients a degree of certainty if their current plans fall through. "I encourage my colleagues to sit with patients and show them you are thinking ahead in terms of their care," he says. "The message should be: This is what we are going to do in each scenario, and we remain available and here to treat and manage your cancer no matter what."

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*Dr. Kalaycio is Vice Chairman of Cleveland Clinic's Taussig Cancer Institute. He can be reached at kalaycm@ccf.org or 216.444.3705. On Twitter: @MattKalaycioMD*

# COMBINATION THERAPY SHOWS PROMISING RESULTS FOR TREATMENT OF SYSTEMIC LIGHT-CHAIN AMYLOIDOSIS

*Primary results from the phase 3 ANDROMEDA study*

**KEY POINTS**

The addition of subcutaneous daratumumab to an existing combination therapy results in superior outcomes for patients with systemic light-chain amyloidosis.

More than half of patients assigned to the daratumumab group achieved a hematologic complete response of 53% compared with only 18% of patients assigned to CyBorD.

The six-month cardiac response rate was 42% for the daratumumab combination compared with 22% for CyBorD alone, and the six-month renal response rates were 54% and 27%, respectively.

The addition of subcutaneous daratumumab to an existing combination therapy results in superior outcomes for patients with systemic light-chain (AL) amyloidosis, according to a recent study. The phase 3 ANDROMEDA study compared adding subcutaneous daratumumab to the combination of cyclophosphamide, bortezomib and dexamethasone (CyBorD) with CyBorD alone.

"This study is the most important in a long time for AL amyloidosis patients," says Jason Valent, MD, Codirector of Cleveland Clinic Cancer Center's Amyloidosis Center. Dr. Valent coauthored the ANDROMEDA study, which was presented at the 25th Congress of the European Hematology Association in the summer of 2020. "Clinical trials and practice-changing studies like this one are advancing the field."

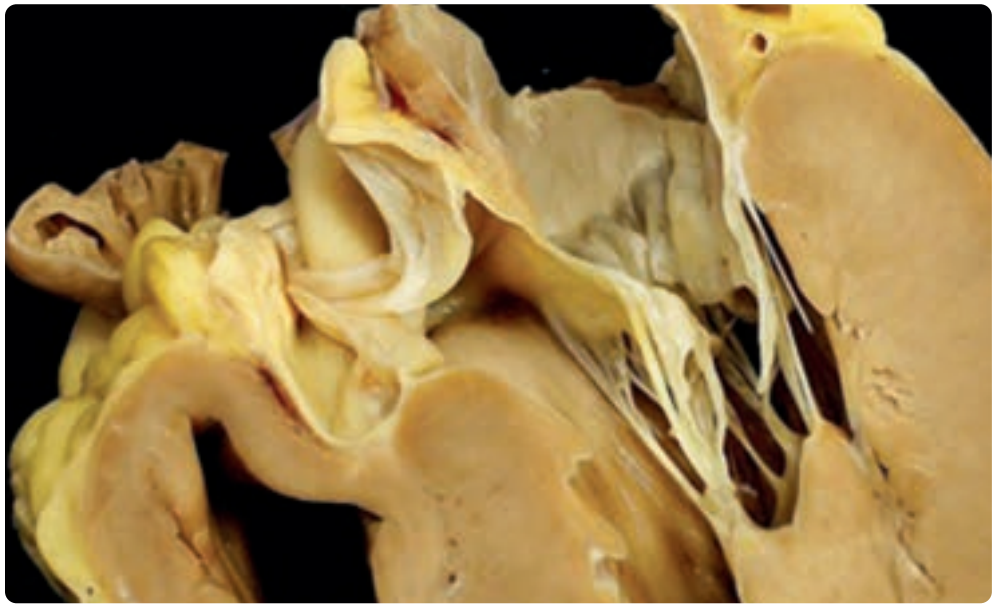
## ANDROMEDA study proves to be practice-changing

The study randomized 388 patients to receive CyBorD alone (N = 193) or with daratumumab (N = 195). The median age was 64 years. Seventy one percent and 59% had heart and kidney involvement, respectively, and 65% had ≥ two organs involved. The primary endpoint was overall hematologic complete response (HCR) rate (intent-to-treat). Secondary endpoints included major organ deterioration progression-free survival, organ response rate, time to hematologic response, survival and safety.

At a follow-up of 11.4 months, the median duration of treatment was more than four months longer in patients assigned to the daratumumab group (9.6 vs. 5.3 months), suggesting that the four-drug combination is tolerable. Nineteen of the patients assigned to daratumumab and 79 patients assigned to CyBorD went on to receive subsequent therapy.

More than half the patients assigned to the daratumumab group achieved an HCR of 53% compared with only 18% of patients assigned to CyBorD (odds ratio, 5.1; 95% CI, 3.2-8.2; $P < 0.0001$). The median time to HCR was 60 days in the daratumumab group versus 85 days for CyBorD alone. The HCR rate at six months was 50% in the daratumumab group versus 14% in the CyBorD group. Treatment with daratumumab was associated with higher rates of overall hematologic response (92% vs. 77%).

Researchers also studied organ response rates. The six-month cardiac response rate was 42% for the daratumumab combination compared with 22% for CyBorD alone ($P = 0.0029$), and



LEFT: Photo of a patient's explanted heart. Note the dramatic thickening of all chambers, which is typical of cardiac amyloidosis.

the six-month renal response rates were 54% and 27%, respectively ($P < 0.0001$). During the study, 56 patients died, 27 in the daratumumab group and 29 in the CyBorD group.

"This study proves that this medication regimen is well tolerated and incredibly effective," says Dr. Valent. "We've seen patients respond positively in as little as two weeks, leading to a better quality of life."

## Amyloidosis Center

Cleveland Clinic's Amyloidosis Center provides leading-edge management and treatment options for patients with amyloidosis. The center focuses on a collaborative approach, with specialist practitioners from hematology/oncology, cardiology, stem cell transplantation, nephrology, neurology, palliative medicine and social work all working together to help patients navigate their treatment course and survivorship.

"Amyloidosis often goes undiagnosed because its symptoms are common to many other conditions. It's mistakenly considered a rare disease, when in fact it is not. In many cases, by the time people with amyloidosis are diagnosed appropriately, they are at the end stage of the disease, when not much can be done," says Dr. Valent. "But the collaborations we're working on now are providing better treatment options and hope for earlier diagnoses."

*Dr. Valent is Codirector of Cleveland Clinic Cancer Center's Amyloidosis Center. He can be reached at valentj3@ccf.org or 216.445.7238.*

# CLINICAL STUDY AIMS TO EVALUATE SCREENING PARADIGM IN HIGH-MORTALITY CANCERS

*Cleveland Clinic joins PATHFINDER, a promising multicenter study*

**KEY POINTS**

Cleveland Clinic has begun enrolling patients in PATHFINDER, a national clinical study designed to evaluate the use of a multicancer early detection test, which can detect more than 50 cancers through a single blood draw.

The previous CCGA study was designed to assess how robust the test is in detecting known cancers, while PATHFINDER is intended to evaluate the care pathways from a cancer "signal detected" test to a diagnosis.

This test is the first step in establishing a new broad-based screening paradigm for lethal cancers and could have a big impact on cancer-related mortality.

Cleveland Clinic has begun enrolling patients in a prospective, national clinical study designed to evaluate the use of a multicancer early detection test, which has demonstrated the ability to detect more than 50 cancers through a single blood draw. When a cancer signal is detected, it's also able to localize the origin of the cancer signal with high accuracy.

The PATHFINDER study marks the first time the test, developed by GRAIL Inc., will be evaluated in clinical practice. Participants include asymptomatic patients who have an average or elevated risk for developing cancer, but no known or suspected malignancy.

Eric A. Klein, MD, Chair of Glickman Urological & Kidney Institute and principal investigator of the Cleveland Clinic arm of the study, is hopeful that this test could serve as a new screening tool for cancers that typically present at more advanced stages, are difficult to treat and lack a broad-based screening paradigm.

Currently, early-detection screening tools exist only for five types of cancer — prostate, cervical, breast, lung and colon. Dr. Klein comments, "There are no equivalent screening resources for many other high-mortality cancers, which account for about 60% of cancer-related deaths in the United States."

## Precursor study demonstrates the test's clinical utility

Findings from GRAIL's Circulating Cell-Free Genome Atlas (CCGA) study, a precursor study to PATHFINDER, demonstrate a high sensitivity rate for the blood-based test. The test's sensitivity was 67.3% for stages I-III of 12 common and deadly cancers including anus, bladder, colon/rectum, esophageal, head and neck, liver/bile duct, lung, lymphoma, ovarian, pancreatic, stomach and plasma cell neoplasm.

Further, the test has a very low false-positive rate (0.7%), meaning that less than 1% of individuals without cancer would be wrongly identified as having cancer. In the 96% of cases when the test was able to predict where the cancer signal originated, its accuracy was 93%.

Simply put, the CCGA study was designed to assess how robust the test is in detecting known cancers, while PATHFINDER is intended to evaluate the care pathways from a cancer "signal detected" test to arriving at a diagnostic resolution.

## Understanding the implications of the test results

The study intends to enroll approximately 6,200 participants across multiple sites and follow them for 12 months. The study is enrolling eligible participants, all age 50 or older, who meet criteria for the two following cohorts: those with no documented risk or history of cancer and those with elevated risk for cancer due to smoking history, previous history of invasive cancer or genetic risk.

LEFT: Eric Klein, MD, the principal investigator of Cleveland Clinic's portion of the PATHFINDER study, meets with a patient.

"Altogether, we expect the prevalence of cancer in our study population to be around 1.41%. If we are correct, then an overwhelming majority of participants are going to have a negative result," says Dr. Klein. "But there are implications for both positive and negative test results."

Positive tests will likely indicate the organ system in which the cancer signal has arisen. This information is intended to inform a diagnostic workup and help physicians develop a subsequent care plan for patients, working hand-in-hand with their primary care provider. As part of the study, investigators will examine physician behavior after results are obtained, such as which tests are ordered and other steps taken to ultimately confirm or deny a cancer diagnosis.

There are short- and long-term implications for negative tests too, stresses Dr. Klein. A negative test may indicate no or a significantly low likelihood of malignancy, but it does not warrant abandonment of routine cancer prevention or screening. "It's critically important that patients continue to work with their primary care physician to get routine screenings for cancers as recommended, like a colonoscopy for colon cancer, chest CT in patients who are at high risk of lung cancer, PSA for prostate cancer, mammography for breast cancer and Pap test for cervical cancer," says Dr. Klein.

With enrollment at Cleveland Clinic now open, Dr. Klein is hopeful that they will have primary data next year. He is even more hopeful about what's ahead.

"Even if this test detects early-stage cancer in a fraction of participants, particularly the notoriously silent and high-mortality cancers like pancreatic and ovarian, it's really the first step in establishing a new broad-based screening paradigm for lethal cancers," he says. "And we think that could have a big impact on cancer-related mortality."

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*Dr. Klein is Chair of Glickman Urological & Kidney Institute.*
*He can be reached at kleine@ccf.org or 216.444.5591.*
*On Twitter: @EricKleinMD*

# SINGLE-FRACTION STEREOTACTIC BODY RADIATION THERAPY EFFECTIVE FOR EARLY STAGE MEDICALLY OPERABLE LUNG CANCER

*Largest retrospective study to date confirms randomized trials*

**KEY POINTS**

SBRT is safe and effective in treating early stage, medically inoperable NSCLC according to a large retrospective study.

The findings of this study validate smaller randomized trials in this patient population.

One fraction is as safe and effective as multiple fractions for this patient population.

Research is ongoing, as lung SBRT is a relatively young practice.

Single-fraction stereotactic body radiation therapy (SBRT) is safe and effective in treating early stage, medically inoperable non-small cell lung cancer (NSCLC), according to Cleveland Clinic's 10-year retrospective study of 229 patients, the largest single-institution report to date in this specific component of lung SBRT.

The study confirms the findings of two smaller, randomized phase 2 trials comparing varying dose/fractionations of SBRT in this patient population.

"It's reassuring to validate previous prospective studies in a large population and know that one fraction remains both safe and effective in the long term," says Gregory M. Videtic, MD, Department of Radiation Oncology, Cleveland Clinic Cancer Center. The findings were presented at the American Society for Radiation Oncology (ASTRO) annual meeting held virtually in late October.

## One fraction versus more: concerns over efficacy

Although the use of SBRT for inoperable early stage lung cancer began about two decades ago, the study of single-fraction (SF)-SBRT only began about 12 years ago in patients with inoperable NSCLC. These medically fragile patients, who are usually former or current smokers, have abnormal pulmonary functions or other comorbidities that make surgery not feasible. They represent only about 5% of all newly diagnosed lung cancer patients, but "we knew they were potentially curable if we could find a way to treat them without harming them with the treatment," says Dr. Videtic.

At Cleveland Clinic, the SBRT program began in 2004 to address this clinical need, and the radiation oncology group began by using a five-fraction schedule for SBRT based on earlier work done in Japan.

But "in the beginning, we were learning 'on the go.' No one knew which SBRT dose schedule or approach was best," says Dr. Videtic. That was why he and his colleagues were very active in taking part in clinical trials over the years where a range of SBRT schedules were tested, including those with four, three and one fractions.

In two multicenter randomized trials — one comparing four fractions with one and the other three fractions with one, published in 2018 and 2019, respectively — one fraction proved as effective as several of fractions and just as safe.

"When we think about it, we are amazed that we can pack an enormous amount of radiation into a single shot that is so focused that it doesn't harm the body around it," Dr. Videtic says.

For routine patients who meet the criteria of the trials, especially having a tumor that is distanced from the central structures of the chest, one fraction SBRT has become the standard of care at Cleveland Clinic. At other centers, however,

LEFT: Dr. Videtic discusses a case.

"some radiation oncologists still have a bit of a psychological hurdle to overcome about using only one fraction, mainly around the safety issue, even though safety and effectiveness were demonstrated in randomized trials. Because Cleveland Clinic is known for its experience in this area, we are frequently contacted by these colleagues at other institutions, seeking guidance and reassurance," says Dr. Videtic.

## Study population and results

The study evaluated 229 patients treated between December 2009 and December 2019 from a Cleveland Clinic prospective data registry. Fifty-five percent of patients were female, with a median age of 74.6 years and median KPS of 80. Over 23% were active smokers. The median pretreatment forced expiratory volume (FEV1) was 1.38L, 58% of predicted, and the diffusing capacity for carbon monoxide (DLCO) was 50% of predicted, with inoperability due to abnormal pulmonary functions in 52.4% of cases. Median tumor diameter was 1.6 cm, and median PET SUV max was 6.1.

The SF-SBRT dose was 34 Gy in 72.1% of cases and 30 Gy in 27.9%, with patient and tumor characteristics balanced between cohorts. At the time of the analysis, 55.9% of patients were alive; the median overall survival time was 44.1 months, with two-year overall survival (OS) at 73.8%. No significant differences in outcomes were identified by dose.

These results were comparable to those of the two randomized clinical trials. In the one versus four fractions trial, the median two-year OS was 61.3% and 77.7%, respectively; in the one versus three fractions trial, the two-year OS was 73% and 62%, respectively.

Clinic radiation oncologists using SBRT still need to build on their experience and document their outcomes to understand the optimum treatment for these patients. "Lung SBRT is still a relatively young practice to be involved in, so analysis of its results has to be ongoing. One of the privileges of working at Cleveland Clinic is having access to a large patient population who can benefit from SBRT and then following them closely for years so you can get a significant sense of how well they have done with time," says Dr. Videtic.

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*Dr. Videtic is staff in the Department of Radiation Oncology. He can be reached at videtig@ccf.org or 216.444.9797.*

# THE ISOPSA TEST COULD CHANGE THE DIAGNOSTIC PARADIGM FOR PROSTATE CANCER

*Clinical indications, how it's filling a void in diagnostic care and more*

**KEY POINTS**

The test is appropriate for patients with a PSA > 4 ng/mL who are facing a decision on prostate biopsy.

Two multicenter, prospective clinical trials validate the superiority of this test compared with PSA assay.

This test offers new clinical data points to guide the physician-patient conversation about prostate cancer biopsy.

Cleveland Clinic is now offering the IsoPSA™ test, a novel prostate-specific antigen assay, for patients with a PSA > 4 ng/mL who are facing a decision on prostate biopsy.

This blood-based diagnostic test has demonstrated superiority over conventional tests in predicting the presence of high-grade prostate cancer, potentially resulting in a significant decrease in unnecessary prostate biopsies, according to Eric Klein, MD, Chair of Cleveland Clinic's Glickman Urological & Kidney Institute.

"Our data show that the IsoPSA test reduces unnecessary prostate biopsies by about 45% by reliably differentiating between the risks of high-grade versus low-grade cancer or benign biopsies," says Dr. Klein.

## Accelerated research to improve clinical care

This most recent development in the availability of the assay follows two multicenter, prospective clinical trials. These studies validate the superiority of this test compared with that of the prostate-specific antigen (PSA) assay, the gold standard for prostate cancer screening and staging.

Developed by the biotechnology company Cleveland Diagnostics Inc.* in partnership with the Urological & Kidney Institute, the technology also received breakthrough device designation from the U.S. Food & Drug Administration in late 2019. This distinction recognizes the clinical significance of the biomarker and should help accelerate regulatory processes, getting tests into the hands of physicians quicker.

## Filling an important need in diagnostic testing for prostate cancer

Conventional PSA testing, the standard-of-care strategy in prostate cancer screening and staging for decades, has demonstrated value as a test for men with higher risk factors, such as age, race and family history.

"Large, randomized trials show that it's a clinically valuable screening test, and it's proven to reduce mortality rates and also reduce the need for treatment of metastatic disease," remarks Dr. Klein. "But it does have limitations, most notably its imprecision when detecting the aggressiveness of the malignancy."

IsoPSA is a reflex test, and it also takes a different biological approach. It interrogates broader, structural changes in a patient's PSA levels as a result of disease pathogenesis, rather than assessing the concentration of the protein. Because the PSA biomarker protein is tissue specific and not cancer specific, it commonly misrepresents protein levels associated with noncancerous conditions, such as benign prostatic hyperplasia or prostatitis. This, as a result, leads to an overdiagnosis of low-grade cancers and an overtreatment of low-mortality tumors. The IsoPSA test overcomes these shortcomings inherent in conventional PSA testing.


LEFT: Now at Cleveland Clinic, the blood-based IsoPSA test demonstrates superiority over conventional tests in predicting the presence of high-grade prostate cancer.

## Integrating the test into clinical practice

Designed to stratify risk of biologically significant prostate cancer (Gleason grade > 7 prostate cancer), IsoPSA is intended to be used in men who are age 50 or older with a total PSA > 4 ng/mL with no previous prostate cancer diagnosis and not under active surveillance.

The test will be piloted within the Cleveland Clinic health system over the next several months. The team overseeing its implementation will be examining best practices and efficiencies in clinical application and specimen processing.

Dr. Klein notes that the team plans to scientifically assess how this test affects clinical practice. He stresses that if used as intended, the test will offer new clinical data points to guide the physician-patient conversation about prostate cancer biopsy.

"The physical, psychological and financial implications of unnecessary biopsy cannot be overlooked. Our goal with this test is to add another piece of evidence to the diagnostic toolkit to help providers and patients make what can be a difficult decision."

Questions about the test can be directed to Dr. Klein (kleine@ccf.org) or Bob Rochelle, MBA, Chief Commercial Officer, Cleveland Diagnostics (bob.rochelle@clevelanddx.com).

* *Cleveland Clinic has an equity position in Cleveland Diagnostics. Dr. Klein has no direct or indirect personal financial interests in the company.*

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# STANDARDIZING CARE FOR CENTRAL NERVOUS SYSTEM LYMPHOMA

*Emerging multidisciplinary program seeks better care, outcomes*

**KEY POINTS**

Cleveland Clinic is establishing a CNS lymphoma transplant program to standardize treatment and accelerate research.

The program will include physicians from hematology/oncology, transplant and neuro-oncology.

Traditional lymphoma therapies can have poor penetration of the blood-brain barrier, so one of the program's goals is to discover the optimal chemotherapy regimen for patients with primary and secondary CNS lymphoma.

Central nervous system (CNS) lymphoma is a rare form of lymphoma that is difficult to treat because so many chemotherapy drugs have poor penetration of the blood-brain barrier. Now an emerging multidisciplinary transplant program at Cleveland Clinic Cancer Center is working to standardize care for this specialized group of patients and to collaborate on new research to better understand the disease.

Patients with CNS lymphoma are typically treated with CNS-penetrating chemotherapy followed by consolidative high-dose chemotherapy (conditioning or preparative chemotherapy) and then autologous stem cell infusion. Only a few conventional, cytotoxic chemotherapy drugs are effective in crossing the blood-brain barrier, and research on which drugs are most effective is lacking.

"There's no one conditioning regimen that's established as the standard, because there are no large, randomized trials comparing them," says Cleveland Clinic oncologist Allison Winter, MD, who is establishing a CNS lymphoma program. Most of the published research is heterogeneous in terms of therapies and patients included and is often limited to phase 2 single-arm and retrospective studies, she notes.

In addition to CNS lymphoma being difficult to treat from a pharmacokinetic/pharmacodynamic perspective, patients and physicians face additional treatment-altering complications including seizures and mobility and cognition problems.

## Standardizing treatment across disciplines

Dr. Winter says she had the idea for a specialized CNS lymphoma program after encountering a case during her hematology/oncology fellowship at Cleveland Clinic, where the neuro-oncology department has historically cared for primary CNS lymphoma patients. "I started wondering if we could collaborate more formally given the emerging data for the use of autologous stem cell transplant for people with primary CNS lymphoma,'" she says.

When she joined the department as staff in 2019, she proposed a collaboration between lymphoma, neuro-oncology and transplant physicians to offer the therapy to patients.

A key goal of the program is to standardize treatment for both primary CNS lymphoma (lymphoma that began in and is limited to the CNS), and secondary CNS lymphoma (systemic lymphoma with CNS involvement or systemic lymphoma relapsed into the CNS). BEAM (BCNU, etoposide, cytarabine and melphalan) is widely used as a standard chemotherapy preparative regimen prior to autologous stem cell infusion for systemic lymphoma, but it has poor penetration of the blood-brain barrier.

For the new CNS lymphoma program, physicians reviewed existing studies and decided on a combination of BCNU (carmustine) and thiotepa for the conditioning chemotherapy. "These are

LEFT: Dr. Allison Winter collaborates with a colleague.

two chemotherapy agents that seem to have a good compromise between safety and efficacy, and they have good penetration into the CNS," Dr. Winter says.

Patients with relapsed systemic lymphoma are traditionally treated with BuCyE (busulfan, cyclophosphamide and etoposide) or BEAM conditioning regimens as noted above. While the transplant program will continue to follow this protocol for most patients, some who relapse exclusively into the CNS could receive the same conditioning chemotherapy as patients with primary CNS lymphoma. That was the case with one patient, whose secondary CNS lymphoma was limited to the CNS, with no systemic involvement.

"It made sense to use this regimen, because that was the only place she relapsed, and I wanted to give her the best CNS-penetrating protocol that I could," Dr. Winter says.

## Stem cell mobilization

The transplant program is also piloting a stem cell mobilization protocol for CNS lymphoma patients. Traditionally, growth factors like filgrastim or chemotherapy such as etoposide are used to mobilize stem cells in systemic lymphoma, but etoposide is less likely to penetrate the blood-brain barrier. Now these patients are being mobilized with cytarabine, a chemotherapy agent with better blood-brain barrier penetration.

Ultimately, Dr. Winter hopes the program will contribute to the small but growing body of knowledge on CNS lymphoma, leading to more effective treatments for the disease. "My long-term goal is to collaborate with more centers, so that we can do larger trials and get better answers and outcomes for these patients, whether that means incorporating novel agents into the transplant process or incorporating novel agents as maintenance after transplant," she says.

*Dr. Winter is staff in the Department of Hematology and Medical Oncology. She can be reached at wintera2@ccf.org or 216.445.4782. On Twitter: @AllisonM_Winter*

# INTRAOPERATIVE PAN-ENTEROSCOPY ON A PATIENT WITH 125 CM OF SMALL BOWEL

*Experts from the Weiss Center treat severe polyposis*

**KEY POINTS**

Weiss Center surgeons used the "clean sweep" procedure to remove 180 polyps from a patient with only 125 cm of small bowel.

Patients with conditions like Peutz-Jeghers syndrome, familial adenomatous polyposis, PTEN hamartoma tumor syndrome, juvenile polyposis syndrome and Lynch syndrome receive comprehensive, coordinated care at the Weiss Center.

The Familial Polyposis Registry includes thousands of patients with these disorders and facilitates proactive screening, surveillance and treatment.

Case Report — A 27-year-old female occupational therapist from Florida presented to Cleveland Clinic with only 125 cm (about 25% of normal) of remaining small bowel after multiple surgeries and resections due to severe polyposis.

She was at risk for short gut syndrome, which is associated with dehydration and malnutrition that may necessitate total parenteral nutrition. She had previously been diagnosed with and surgically treated for Peutz-Jeghers Syndrome (PJS), a hereditary colorectal cancer syndrome that causes hamartomatous polyps, an elevated lifetime cancer risk of 37% to 93% and mucocutaneous pigmentation.

"She came to us with few surgical options remaining," said David Liska, MD, Director of the Sanford R. Weiss, MD, Center for Hereditary Colorectal Neoplasia at Cleveland Clinic's Digestive Disease & Surgery Institute. "She was not followed by a registry and so did not have appropriate surveillance."

Weiss Center caregivers performed an MR enterography that showed massive polyposis of the small bowel. Endoscopic removal was attempted, but adhesions from previous surgeries prevented necessary endoscopic access. Instead, Amit Bhatt, MD, and Dr. Liska performed a "clean sweep," or intraoperative pan-enteroscopy, a procedure that removes polyps inaccessible on balloon enteroscopy.

"Although she had only 125 cm of small bowel left, we successfully removed 180 polyps through this combined approach, and allowed her to keep her small bowel," notes Dr. Bhatt, an advanced endoscopy specialist with the Weiss Center.

"That's an extraordinary number, and would only be possible through this team approach. Fortunately none of them were cancerous polyps."

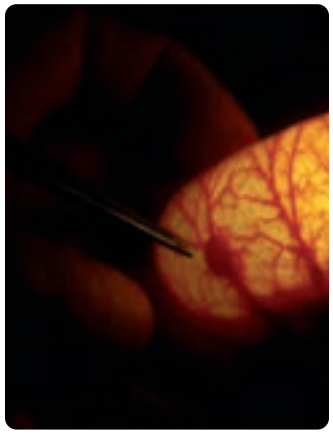
The patient is doing well and is returning to the Weiss Center for another procedure. Her brother is now a patient as well.

## Hereditary colorectal neoplasia

Patients with PJS are often diagnosed in middle childhood or the early teen years and present needing emergency surgery for small bowel obstruction due to polyposis-related intussusception and resulting in bowel ischemia or necrosis. "These patients often require several surgeries over the years," notes Dr. Liska. "At the Weiss Center, we have a registry that allows us to follow patients very closely to avoid emergency procedures and instead use prophylactic measures to prevent bowel obstructions and cancer."

Since patients with PJS are also predisposed to several types of cancer, the Weiss Center coordinates screening and surveillance so that cancers can be diagnosed and treated early. The multidisciplinary center's mission is to prevent death or complications from cancer and to maintain quality of life for patients with hereditary colorectal conditions. Other syndromes of hereditary colorectal neoplasia include familial adenomatous polyposis, PTEN hamartoma tumor syndrome, juvenile polyposis syndrome and Lynch syndrome.

IMAGE 1



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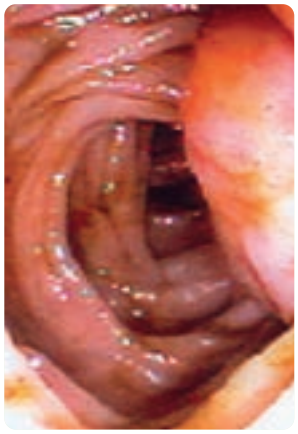

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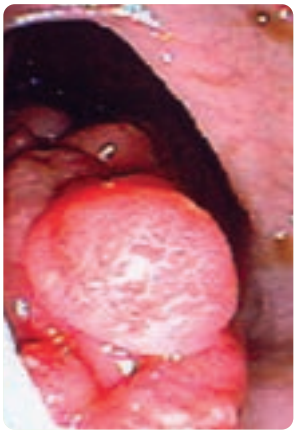

IMAGE 1: Intraoperative enteroscopy transilluminating the small bowel with the silhouette of a polyp outlined.

IMAGES 2 and 3: The endoscopic appearance of PJS polyps.

## The "clean sweep"

Patients with PJS are at increased risk for intestinal cancer and at high risk for bowel obstructions. The Weiss Center team monitors patients for polyps via enterography and capsule endoscopy with the hope that polyps can be removed endoscopically before they get big enough to cause obstruction or to develop into cancers.

"Sometimes, as in our patient from Florida, they simply cannot be totally removed endoscopically for various reasons," says Dr. Bhatt. "Then, we use an advanced, team-based method in the OR that allows us to view the entire intestine from mouth to anus using manually guided intraoperative endoscopy to remove polyps and prevent obstructions or cancer."

James Church, MD, the Weiss Center's first director, nicknamed this procedure the "clean sweep." A recent study of 50 Cleveland Clinic patients demonstrated that this procedure decreases the need for emergency laparotomies for small bowel obstruction due to polyp-related intussusception in patients with PJS. Further studies are planned to confirm these results.

## The Weiss Center and the Jagelman registry

These studies all draw from a ground-breaking concept. In 1979, Dr. David G. Jagelman established Cleveland Clinic's Familial Polyposis Registry. His intent was to follow high-risk colorectal patients and families with a personal and/or family history of familial adenomatous polyposis and other similar syndromes. In 1989, hereditary nonpolyposis colorectal cancer was added to the registry.

"Now the registry includes thousands of patients and their families and has allowed us to learn more about the best ways to track and treat these disorders," says Dr. Liska. For instance, the registry's presence promotes proactive screening for Lynch syndrome. The Digestive Disease & Surgery Institute, Genomic Medicine Institute, Pathology and Laboratory Medicine Institute and Women's Health Institute collaborate through the Weiss Center to provide comprehensive and coordinated risk-based screening, surveillance and treatment for patients with Lynch syndrome.

Because these hereditary syndromes are so rare, the Weiss Center receives referrals from all over the world. "We are a one-stop shop for patients. Patients from out of town can get all of their visits in a single day, and we employ three full-time coordinators to ensure the referral process is as easy as possible for physicians and patients."

To refer a patient to the Weiss Center please call 216.444.6470, e-mail WeissCenter@ccf.org or visit clevelandclinic.org/Weiss.

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*Dr. Bhatt is an advanced endoscopy specialist with the Weiss Center. He can be reached at bhatta3@ccf.org or 216.444.9246. On Twitter: @amitbhattMD*

# CLEVELAND CLINIC CANCER CENTER UPDATES

## NEW STAFF

Vivek V. Abhyankar, MD, joined Cleveland Clinic Cancer Center in Sandusky. Dr. Abhyankar previously served as a hematologist and medical oncologist at Strecker Cancer Center in Marietta, Ohio.

Brian Haines, MD, joined the Department of Hematology and Medical Oncology after completing fellowship at the University of Cincinnati. He sees patients at Cleveland Clinic Cancer Center at Fairview Hospital and Avon Hospital.

Jae Jung, PhD, has been appointed Chair of Lerner Research Institute's Department of Cancer Biology. Dr. Jung will also serve as Director of the new Center for Global and Emerging Pathogens Research.

Ruth Keri, PhD, has joined Cleveland Clinic Lerner Research Institute's Department of Cancer Biology, where she will study breast cancer, focusing on identifying the molecular processes that control the formation of breast cancers and their metastasis.

Bahar Laderian, MD, has joined the Cleveland Clinic gastrointestinal cancer team after completing fellowship at Columbia University Medical Center, New York Presbyterian Hospital. Dr. Laderian is a recipient of the Conquer Cancer Foundation's Young Investigator Award.

Ahed Makhoul, MD, joined the Department of Palliative & Supportive Care. Dr. Makhoul completed his internal medicine residency and hospice and palliative medicine fellowship at Cleveland Clinic.

Sandy Mazzoni, DO, joined the nonmalignant hematology team after completing her fellowship at the Medical University of South Carolina. She sees patients with benign hematologic disorders and multiple myeloma.

Pradnya Patil, MD, is the newest member of the Cleveland Clinic lung cancer program after completing her fellowship in hematology/oncology at Cleveland Clinic. She will be seeing patients with thoracic malignancies and leading a clinical research program in immunotherapy in lung cancer.

## CURRENT STAFF ROLE UPDATES

Hetty Carraway, MD, MBA, has been appointed Director of Cleveland Clinic Cancer Center's Leukemia Program. She is also Vice Chair of Strategy and Enterprise Development for Taussig Cancer Institute.

Aaron Gerds, MD, has been appointed Deputy Director for Clinical Research. Dr. Gerds serves as the principal investigator for a number of clinical trials for the treatment of myeloproliferative neoplasms and is focused on developing novel therapies for these patients.

David Liska, MD, MA, has been appointed Director of the Sanford R. Weiss, MD, Center for Hereditary Colorectal Neoplasia and Program Director for the James Church, MD, and Sheetz Family Endowed Clinical Fellowship in Hereditary Colorectal Cancer Syndromes.

Navneet Majhail, MD, MS, has been appointed Vice Chair of Cleveland Clinic Cancer Center's Department of Hematology and Medical Oncology. He has served as Director of Cleveland Clinic's Blood & Marrow Transplant Program.

Nathan Pennell, MD, PhD, has assumed the role of Vice Chair of Clinical Research at Cleveland Clinic Cancer Center. He has served as Director of Cleveland Clinic's Lung Cancer Medical Oncology Program.

Laura Shoemaker, DO, has been appointed the inaugural Chair of the Department of Palliative & Supportive Care founded in 2020 by Cleveland Clinic's Board of Governors.


## CLEVELAND CLINIC CANCER CENTER SPEAKERS BUREAU

Cleveland Clinic Cancer Center Speakers Bureau offers a full range of oncology topics presented by various industry-leading experts working in our Cancer Center. Educational sessions are available virtually to physicians, nurses, hospitals and healthcare professionals during Tumor Boards, Grand Rounds and other virtual meetings. Past topics have included management of the late effects of cancer treatment, circulating tumor cells and renal cell advancements.

To customize a virtual speaker's program for your organization's specific needs or to learn more, email Jamie Hundorfean at ryanjam@ccf.org.

## VELOSANO GOES VIRTUAL IN 2020

VeloSano (Latin for "swift cure") is a year-round fundraiser benefiting cancer research at Cleveland Clinic. It has raised more than $24 million since its inception in 2014. In the past, the initiative would feature a "Bike to Cure" weekend in July. Amid the pandemic, however, a gathering that typically attracts more than 2,400 riders and 1,000 volunteers just wasn't possible in 2020 — so VeloSano went virtual this year. Participants were able to take part from anywhere in the world, in any way they could. No bike? No problem. Whether they walked, swam, ran or even embroidered, the mission was the same: to provide critical funding for lifesaving cancer research.

Virtual VeloSano resulted in over 2,900 participants representing 39 states and six countries, and over 18,000 donations were received, for a grand total of $3 million raised in 2020. Every dollar directly benefits Cleveland Clinic in the research areas of cancer genomics, immunotherapy and clinical trials. The research supported by Virtual VeloSano will be announced in early 2021.

VeloSano 8 "Bike to Cure" weekend is scheduled for July 16-18, 2021. Learn more and get involved at **velosano.org**.

# THE CANCER CENTER AND CLEVELAND CLINIC'S CENTENNIAL

*Reflecting on our progress and potential*

by Brian Bolwell, MD

As Cleveland Clinic celebrates 100 years of medical innovation and leadership in 2021, I can't help but reflect on the immense changes that have occurred in cancer care in just the past decade or so. Cleveland Clinic Cancer Center has changed in two fundamental ways over the past 10 years.

First, we changed how we are organized to focus on cancer programming. Each cancer program is a disease-based team comprising physicians from different specialties as well as nurses and other support staff. Team-based care for each cancer diagnosis is critical. Programming allows us to prioritize and structure different aspects of team-based care, including multidisciplinary clinics, tumor boards, care paths and reduction in time to treat. It's a natural evolution of the group practice model Cleveland Clinic pioneered in 1921.

Second, cancer care in general has experienced major clinical shifts in both how we classify and treat cancers. Now instead of naming a cancer based solely on how it looks under a microscope, almost all cancer diagnoses these days are based on genomic or immunological abnormalities. This is a substantial change that has contributed to a paradigm shift in cancer therapeutics.

In recent years, immunological and genomic therapies have increasingly become the standard of care. Ten years ago, these therapies were standard in a few cancers, and now they are part of care paths for a majority of cancers. The successes we're seeing with this approach are heartening to those of us who treated patients in a time before they were available. The outcomes of immunologic therapies for diseases like melanoma and renal and lung cancers, among many others, are a springboard for more optimism about where the next 10 years could take us. Our recently founded Center for Immunotherapy and Precision Immuno-Oncology will transform that optimism into action.

The other form of immunologic therapy that is generating major clinical improvement is cellular therapy, especially for hematological malignancies. Cleveland Clinic Cancer Center was part of a phase 2 trial of chimeric antigen-receptor T-cell therapies for large B-cell lymphoma and continues to engage in both clinical and basic research about this therapy. While it remains to be seen where successes will be found in the multitude of studies looking at cellular therapy for solid tumors, there will be exciting successes for our patients.

Finally, the innovations of the past few years have presented us with a new but welcome problem: survivorship. The advent of immunologic and, to some extent, genomic therapies have allowed people to live with cancer as a chronic disease. The implications of an increasingly large number of people living with cancer are wide ranging, from the development of additional abnormalities due to the interplay between immunologic drugs and genomic abnormalities to the unknowns of long-term use of immunologic agents. Our researchers and clinicians are on the forefront of addressing these issues as they evolve over the coming years.

The world of cancer care is indeed very different than when many of us joined the field years ago, and the possibilities are striking and extraordinarily promising for our patients. That statement is not based solely in hope, but in the factual outcomes of the scientific advances of the past 20 or so years. We all have many years of discovery to look forward to as we build on a 100-year tradition of leadership in scientific innovation at Cleveland Clinic.

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*Dr. Bolwell is Chair of Taussig Cancer Institute and Cleveland Clinic Cancer Center. He can be reached at bolwelb@ccf.org or 216.444.6922. On Twitter: @BrianBolwellMD*

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*An interview-style podcast hosted by Dr. Brian Bolwell and featuring experiences, challenges, successes and insights from leaders working at Cleveland Clinic and organizations around the globe. clevelandclinic.org/beyondleadership*

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## ABOUT CLEVELAND CLINIC

Cleveland Clinic is a nonprofit, multispecialty academic medical center integrating outpatient and hospital care with research and education for better patient outcomes and experience. More than 4,500 staff physicians and researchers provide services through 20 patient-centered institutes. Cleveland Clinic is a 6,026-bed healthcare system with a main campus in Cleveland, 18 hospitals and over 220 outpatient locations. The health system includes five hospitals in Southeast Florida with more than 1,000 beds, a medical center for brain health in Las Vegas, a sports and executive health center in Toronto, and a 364-bed hospital in Abu Dhabi. Cleveland Clinic London, a 184-bed hospital, will open in 2022. Cleveland Clinic is currently ranked as one of the nation's top hospitals by *U.S. News & World Report*.

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