

A Neuroendocrine Tumor Specialty Center in New Orleans' (NOLANETS) Response to Patient Care During the COVID-19 Pandemic

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Disclosures of potential conflicts of interest may be found at the end of this article.

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INTRODUCTION

On December 31, 2019, China reported a cluster of cases of pneumonia, of initially unknown cause, in people associated with the Huanan Seafood Wholesale Market in Wuhan, Hubei Province [1]. On January 7, 2020, the Chinese health authorities confirmed that this cluster of cases was associated with a novel coronavirus—later termed SARS-CoV-2 [2]. Tracing of the global outbreak indicates that the last week of January was pivotal for the international spread of the virus. Over the course of a week, the number of affected countries increased from 7 to 20, while the number of confirmed cases outside of China increased almost 10-fold (from 11 to 106).

On January 20, 2020, the Centers for Disease Control and Prevention (CDC) confirmed that a 35-year-old man who presented to an urgent care clinic in Snohomish County, Washington, tested positive for SARS-CoV-2, and on February 26, 2020, the CDC confirmed an infection with SARS-CoV-2 in California in a person who reportedly did not have relevant travel history or exposure to another known patient with COVID-19 (the disease caused by SARS-CoV-2), indicating community spread of the virus. At this time point, the total number of COVID-19 cases in the U.S. was 15 [3]. As of April 7, 2020, there were 368,844 confirmed cases and 11,033 COVID-19-related deaths in the U.S. [4].

Louisiana reported its first presumptive case of COVID-19 on March 9, 2020. Since then, the outbreak in Louisiana, particularly in the New Orleans metro area, has grown at an alarming rate, with 14,867 confirmed cases and 512 deaths as of April 6, 2020 [5]. As the state expanded testing for SARS-CoV-2, a University of Louisiana at Lafayette study estimated that the growth rate in Louisiana was among the highest in the

world, prompting serious concerns about the state's health care capacity to care for critically ill patients [6]. As of April 6, 2020, intensive care unit (ICU) beds were at near capacity in the New Orleans metro area, and Governor John Bel Edwards announced that the state was projected to run out of ventilators by April 9, 2020, and ICU beds by April 10 [7].

Based upon available information to date, the CDC has identified those at high risk for severe illness from COVID-19 to include people aged 65 years and older as well as people who live in a nursing home or long-term care facility. Patients with cancer may also be at higher risk of contracting the virus and having more severe symptoms [8]. Other high-risk conditions include (a) individuals with chronic lung disease or moderate to severe asthma; (b) individuals who have serious heart conditions; (c) individuals who are immunocompromised, including those receiving cancer treatment; (d) individuals of any age with severe obesity (body mass index ≥ 40); (e) individuals with underlying medical conditions, particularly if not well controlled, such as diabetes, renal failure, or liver disease; and (f) women who are pregnant, should be closely monitored [9].

The New Orleans Louisiana Neuroendocrine Tumor Specialists (NOLANETS) is a high-volume specialty referral center for patients with all types of neuroendocrine tumors (NETs). Our center, a collaboration between Ochsner Medical Center and the Louisiana State University Health Sciences Center, has seen more than 3,000 cases of NETs from around the U.S. and internationally. Given the high risk to our patient population and the need to minimize possible exposure to SARS-CoV-2, our institution has implemented new guidelines for NET patient care during this crisis. We have stratified our patients

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in an attempt to weigh the risks and benefits of continuing standard care versus delaying treatment. Given the current pandemic, and proximity to New Orleans, we have tried to delay face-to-face visits with clinic physicians by providing the opportunity for virtual visits with the goal of 90% of patients being seen virtually as opposed to face to face, recognizing that this may not always be possible. Virtual visits are accomplished using (a) established video conference through the electronic medical record (EMR) video platform, (b) a telephone in those patients unable to use EMR, or (c) a third-party video conference with the patient informed of the potential breach of confidentiality (i.e., FaceTime, Skype).

Patients within the state of Louisiana are offered virtual visits through one of the platforms described. A significant number of our patients, however, come from outside of Louisiana, and the usual regulations allowed physicians to practice telemedicine only in a state in which they were licensed. On March 13, 2020, President Donald Trump declared a Proclamation of National Emergency that loosened some regulations regarding physicians practicing outside of the state they are licensed to practice in (although final approval is up to individual states) [10]. This proclamation opened the door for patients who usually travel for other specialty care to be “seen” through one of the virtual platforms, so that they could either continue their specialty care or establish care.

The following guidelines are being used at NOLANETS to minimize the near-term exposure to SARS-CoV-2, while maximizing long-term successful patient outcome during the ongoing COVID-19 pandemic.

INTAKE FOR NEW PATIENTS AND INITIATION OF TREATMENT

Our center uses neuroendocrine nurse navigators to triage patients with the correct physician (i.e., medical oncologist, surgical oncologist, nuclear medicine, etc.), and they are usually the first point of contact with our clinic. The navigators also secure outpatient medical records and schedule patients for scans, which may include computed tomography (CT), magnetic resonance imaging, or gallium 68 DOTATATE positron emission tomography/CT along with neuroendocrine-specific tumor markers. Some of these modalities are only available in a specialty center, and because we recognize the limitations of outside institutions regarding timing for imaging and availability on a usual basis, we understand that some information may be missing. Our nurse navigator’s role would be to gather the critical information prior to a virtual visit to include pathology, pertinent labs, and scan results when possible. The patient is then scheduled with the appropriate physician who meets with the patient virtually.

During a new patient virtual visit, the physician reviews the patient’s medical history and diagnosis of NET and determines treatment options as being either curative for early-stage or palliative for advanced-stage patients. For early-stage patients for whom curative intent surgery is indicated, these patients are being delayed and reassessed at 30–45 days from the initial visit. As we do not know the timing of the pandemic, patients may be referred to other specialty centers where the virus is less endemic.

For advanced-stage patients, treatment initiation is determined by several factors including grade, symptoms, and

burden of disease. Neuroendocrine tumors fall into one of three grades as determined by the World Health Organization (WHO) classification [11, 12]. Because several therapies used for treatment of NETs can create an increased susceptibility to infection, patients with a low burden of disease and who are asymptomatic can be delayed from initiation of new treatment. For patients with low- or intermediate-grade NETs, long-acting somatostatin analogs (SSAs) have been the backbone treatment and are used for not only tumor control but also symptom control from carcinoid syndrome [13–15]. For new patients who have not yet been initiated on treatment with an SSA, and who do not have symptoms of carcinoid syndrome, we are delaying the start of treatment to limit the exposure to the patient. If, however, the patient does have carcinoid syndrome that is not controlled with a short-acting SSA, then we would discuss initiation of a long-acting SSA at their home oncology center.

For those patients with grade 1 or 2 NETs who require targeted treatment beyond an SSA, the choice of treatment should be individualized. Both everolimus and sunitinib are indicated for patients with pancreatic NETs, and everolimus also has additional indications for gastrointestinal and lung NETs [16–18]. Although both of these agents are effective, they each have potential toxicity that needs to be taken into account prior to initiation, and patients need to be monitored closely throughout treatment. For instance, both sunitinib and everolimus can produce lymphopenia and neutropenia that could result in infections, including viral infections. Additionally, pneumonitis has been reported in patients on treatment with everolimus, which can mimic symptoms of COVID-19 including cough, dyspnea, and fever. Patients and physicians need to be aware of these potential adverse events and be vigilant about symptom and lab monitoring. If the disease burden is low and the patient is asymptomatic, then we would generally hold the initiation of treatment.

Grade 3 NETs are classified as either well differentiated or poorly differentiated by the WHO classification [11, 12]. Both classifications can be clinically aggressive, and because of this, treatment should be offered sooner rather than later, but it may be delayed depending on the burden of disease, as well as symptoms. For advanced, well-differentiated, high-grade NETs, we advocate for the use of oral oncolytics wherever possible, such as combination capecitabine and temozolomide [19]. Like targeted therapy, adverse effects are possible, including myelosuppression, and therefore, this regimen will need to be closely monitored with routine labs, and dose adjustments may need to be made accordingly. For advanced, poorly differentiated, grade 3 neuroendocrine carcinomas, platinum-based chemotherapy is still the first-line standard of care, and we recommend treatment to begin as soon as reasonably possible. These regimens are also known to be myelosuppressive, and therefore, extra care should be taken to ensure the patient has the least risk to exposure. For instance, oral etoposide should be considered rather than intravenous (IV) to limit infusion center contact.

SCHEDULING ESTABLISHED PATIENTS AND TREATMENT WITH SSA, TARGETED THERAPY, OR CHEMOTHERAPY

Similarly to scheduling new patient visits, either our physician nurse or nurse navigator is a coordinator of this process. We

are making every effort to see these patients through a virtual visit. For those patients who have low- or intermediate-grade NETs, and for whom prior surveillance imaging had indicated no evidence of disease, we are delaying scans and tumor markers for 3 months before reassessing need. For those patients with advanced disease who are currently on treatment with an SSA or targeted therapy (i.e., everolimus), we are also delaying scans but would recommend continuing on the SSA if this can be done at their home oncology center (if this can be done with limited exposure). For patients with well-differentiated, grade 3 neuroendocrine tumors who have been stable on treatment previously, we are delaying scans at least 1 month and reassessing conditions at that time; however, if the new regimen was started within the last 3 months, we will continue with the previously scheduled imaging. For those patients with poorly differentiated, grade 3 neuroendocrine carcinomas, we will continue surveillance scans and treatment as usual. Whenever possible, scans should be done locally and forwarded to our center to be reviewed in tumor board with recommendations communicated to the referring physician and patient.

RADIONUCLIDE THERAPY

Treatment with peptide receptor radionuclide therapy using Lu-177 is a standard practice at our institution for patients with NETs who have progressive disease on an SSA [20]. This treatment is delivered at 8-week intervals within our infusion center for a total of four cycles. During this pandemic, we are delaying existing patient treatment for 8 weeks and reassessing in patients with grade 1 or 2 NETs who are asymptomatic or have low volume of disease. Additionally, those patients with low burden of disease who are asymptomatic and who have not started treatment will be delayed and reassessed 8 weeks later. For patients who are symptomatic or have high-volume disease, we will continue on with existing treatment and may initiate new treatment, but we will limit clinic contact and infusion center exposure as much as possible through virtual follow-up visits. Although it is possible that less than the planned four cycles may be equally effective, this has not yet been established in a prospective trial but could be considered on an individual basis.

CLINICAL TRIALS

Clinical trials may provide new options for treatment or supportive care for many of our patients with NETs. That said, unlike standard treatment, there are many additional layers involved in starting a patient on a clinical trial that require multiple different personnel including nurses, clinical research coordinators, monitors, and regulators. During this pandemic, multiple personnel have been working from home and resources are limited. Additionally, there is an increased clinical volume for investigators. Therefore, initiation of patients on clinical trials will be limited to only those patients who have no other reasonable options or who would likely derive significant benefit from participation. In this patient population, the investigator will have an increased role in the consenting process and the initiation of the patient on trial. Support staff are still involved but work remotely and can provide virtual visits with the patient. Patients who are currently enrolled in clinical

trials will continue as scheduled even though clinic visits have been moved to virtual visits.

LIVER-DIRECTED THERAPY

Transarterial chemoembolization, bland embolization, radioembolization, and ablation are all modalities used to treat patients with NETs with significant liver disease. Patients are discussed in a multidisciplinary tumor board prior to initiation of any liver-directed therapy. For now, those patients with a low-burden hepatic metastatic disease who are asymptomatic can be deferred for at least 8 weeks. For those patients who need immediate treatment, we are offering a virtual preprocedure visit and preferred outpatient embolization whenever possible. This includes performing the procedure in the morning and keeping the patient in the postprocedure holding area until it is felt safe for them to be discharged. Only those patients with severe symptoms after the procedure would be admitted for further observation or treatment. We have established the infrastructure for IV fluids and antiemetics to be given in the infusion center next to our clinic for patients who need intermittent fluids to treat postembolization syndrome in the days following the procedure. This has allowed us to manage patients in the outpatient setting who would have previously been admitted for observation and similar IV intervention.

SURGERY

Surgery is the only known curative modality for patients with NETs. These oncologic surgeries are often complex and require a significant amount of resources, including postoperative care in the intensive care unit. During this pandemic, elective operations, including curative intent operations and cytoreductive surgeries, are being delayed 30-45 days before reassessing conditions. Urgent surgeries that cannot reasonably wait 30-45 days are being evaluated on a case-by-case basis. Emergent surgery will not be delayed.

ENDOSCOPY

The use of colonoscopy, esophagogastroduodenoscopy, and endoscopic ultrasound are mainstays of endoscopy for the diagnosis and treatment of certain NETs. Most of the time, however, these procedures are deemed to be elective and therefore at this time are likely to be delayed. Certainly, emergent procedures would continue, for example, in patients who develop gastrointestinal bleeding. Endoscopic retrograde cholangiopancreatography is a separate procedure that may be useful in treating a blockage of the biliary tract, and we are currently continuing with this procedure on a case-by-case basis.

NUTRITION

We routinely use a dietitian because many patients with NETs have ongoing nutritional deficiencies. During usual care, our dietitian will meet with the patient in conjunction with their physician appointment. At this time, our dietitian is assessing the nutritional parameters remotely and contacting the patient through one of the virtual platforms for recommendations.

PATIENT EDUCATION AND SUPPORT

We recognize that a cancer diagnosis and care can provoke significant anxiety in patients and caregivers. Throughout our virtual visits, we have tried to educate patients and caregivers as to the most recent CDC guidelines for prevention of COVID-19 [21]. We also have an EMR where patients can send questions to their treatment team, which are answered that same day. We have added additional information on our social media platform and website and have continued to update this on a regular basis as new information and guidelines become available.

CONCLUSION

Patients with neuroendocrine tumors are a heterogeneous population with multiple treatment options and unique needs. We have established these guidelines to help our center and others who treat patients with NETs during this tense time to continue to care for patients. These guidelines continue to evolve as we learn more about COVID-19, but we remain vigilant in trying to provide the best care for our patients, while also protecting our staff.

This pandemic has taught us that we need to think outside of the box in caring for patients with rare diseases. The federal government's loosening of regulations regarding telehealth has certainly helped provide a platform so that patients do not need to travel long distances and risk

exposure but still maintain a high level of expert care. This model could potentially be applied to other types of rare diseases that require specialty center care and for patients who are unable to obtain expert care locally or unable to travel.

Although this current situation is fluid, and there are still many unanswered questions regarding the COVID-19 pandemic, it is likely that this will change specialty cancer care in the future. In our experience, most patients, as well as the treatment team, have adapted quickly to the virtual visit platform. It is conceivable that patients would prefer to have their care done this way in the future. Through telehealth and virtual visits, many specialty services could potentially be delivered without sacrificing outcomes and possibly increasing patient satisfaction. Prospective trials should be designed that could help answer this question in the future.

DISCLOSURES

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