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The Role of Advanced Practice Providers and Telemedicine in Reinventing Care: The Transition of a CAR T-Cell Transplantation Program to the Outpatient Setting

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Abstract

As the health-care industry continues to be pushed to find new, innovative ways to deliver quality care with an emphasis on enhancing quality of life, the use of advanced practice providers and telemedicine technology are two promising developments at the forefront of this new era. Advanced practice providers have been shown to provide highly effective, quality patient care. They often deliver this care at a decreased cost to the patient and healthcare system. Telemedicine technology allows providers to access patients through new, patient-centered avenues, thus enhancing their healthcare experience. Advanced practice providers are well equipped to apply telemedicine technology to expand access to care and innovate new care delivery models. This article describes the design and implementation of a novel telemedicine care model within a malignant hematologic team.

Cellular therapy is a growing field of cancer treatment (Lamprecht & Dansereau, 2019). Chimeric antigen receptor (CAR) T-cell therapy is perhaps the most notable and promising of these cellular therapies. CAR T-cell therapy utilizes a patient's own immune T cells to target antigen(s) in an effort to eradicate the malignancy while preserving a patient's healthy cells (Lamprecht & Dansereau, 2019). The efficacy of this therapy depends on the quality of interaction between the CAR T cell and its target(s). Early clinical trials of CAR T-cell therapy showed com-

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plete responses in approximately 40% to 60% of patients treated—many of whom previously had very few treatment options (Sermer & Brentjens, 2019). Given the remarkable success of CAR T-cell therapy, two drugs targeting CD19 receptors received U.S. Food & Drug Administration (FDA) approval in 2017 for the treatment of acute lymphoblastic leukemia (ALL) and relapsed or refractory diffuse large B-cell lymphoma (DLBCL; Lamprecht & Dansereau, 2019). This article reviews the development and initiation of an innovative model of care in an urban academic medical center that became one of the few authorized CAR T-cell therapy treatment centers in the United States. Additionally, this center became the only center in a seven-state region of the Southeast approved to administer the first FDA-approved CAR-T cellular therapy for the treatment of adult patients with relapsed or refractory DLBCL.

THE INNOVATION

Despite the astounding success of CAR T-cell therapy in patients who previously had limited treatment options, one of the major concerns in the delivery of CAR T-cell therapy is its distinctive and possibly life-threatening toxicities (Sermer & Brentjens, 2019). The most common side effects are cytokine release syndrome (CRS) and neurotoxicity. Notably, the CRS seen in CAR T-cell therapy is distinct in its progression compared to CRS noted in other therapies such as blinatumomab. Historically, patients receiving commercial CAR T-cell therapy products have been treated in the inpatient setting due to concerns for these unique toxicities and the potentially rapid progression from mild to severe symptoms requiring elevated levels of care.

A multidisciplinary and multidepartmental team consisting of physicians, advanced practice providers (APPs), pharmacists, registered nurses, and social workers spanning inpatient, outpatient, and emergency departments (EDs) was assembled to assess the current state of our commercial CAR T-cell therapy program and identify opportunities to safely improve patient experience (Figure 1). This group identified an opportunity to utilize a preexisting outpatient bone marrow transplant (BMT) program model, telemedicine resources, and APPs to deliver CAR T-cell therapy to a select subset of patients within a novel outpatient telehealth care delivery model.

As defined by the Human Resources & Services Administration, "Telehealth is the use of electronic information and telecommunications technologies to support and promote long-distance clinical health care, patient and professional health-related education, public health and health administration" (2019). Traditionally, telehealth is used to assist health-care providers in overcoming barriers by providing remote access to patients, common in underserved or under-resourced communities (Rutledge, Haney, Bordelon, Renaud, & Fowler, 2014). Within our care delivery model, telehealth allows providers to assess patients in real time, allowing patients the newest cancer treatment while having increased quality of life outside the hospital.

The key components of the outpatient telemedicine CAR T-cell therapy program include outpatient clinic capacity, infusion center, 24/7 specialized inpatient APP and physician team, dedicated 24/7 cellular phone exclusively for CAR T-cell therapy patients, integration of encrypted video teleconferencing within electronic health record (EHR), streamlined direct admission process to a specialized inpatient unit, and ED workflow to allow for rapid triage of CAR T-cell therapy patients presenting to the ED. These key components are necessary for strong continuity of care with patient safety at the utmost priority.

ADVANCED PRACTICE PROVIDERS AS DRIVERS

The inpatient Hematology, Oncology, and BMT service is covered 24 hours a day by both physicians and APPs who are specialized to work with this subset of patients. In addition to providing high-quality, safe, and evidence-based patient care, APPs in inpatient settings have been proven to generate revenue, decrease overall hospital length of stays, and provide patients with consistent and standardized care (Kapu, Kleinpell, & Pilon, 2014).

Once a patient's eligibility for CAR T-cell therapy is noted, a pretransplant/cellular therapy APP coordinates the necessary pretransplant workup prior to CAR T-cell infusion. This may include

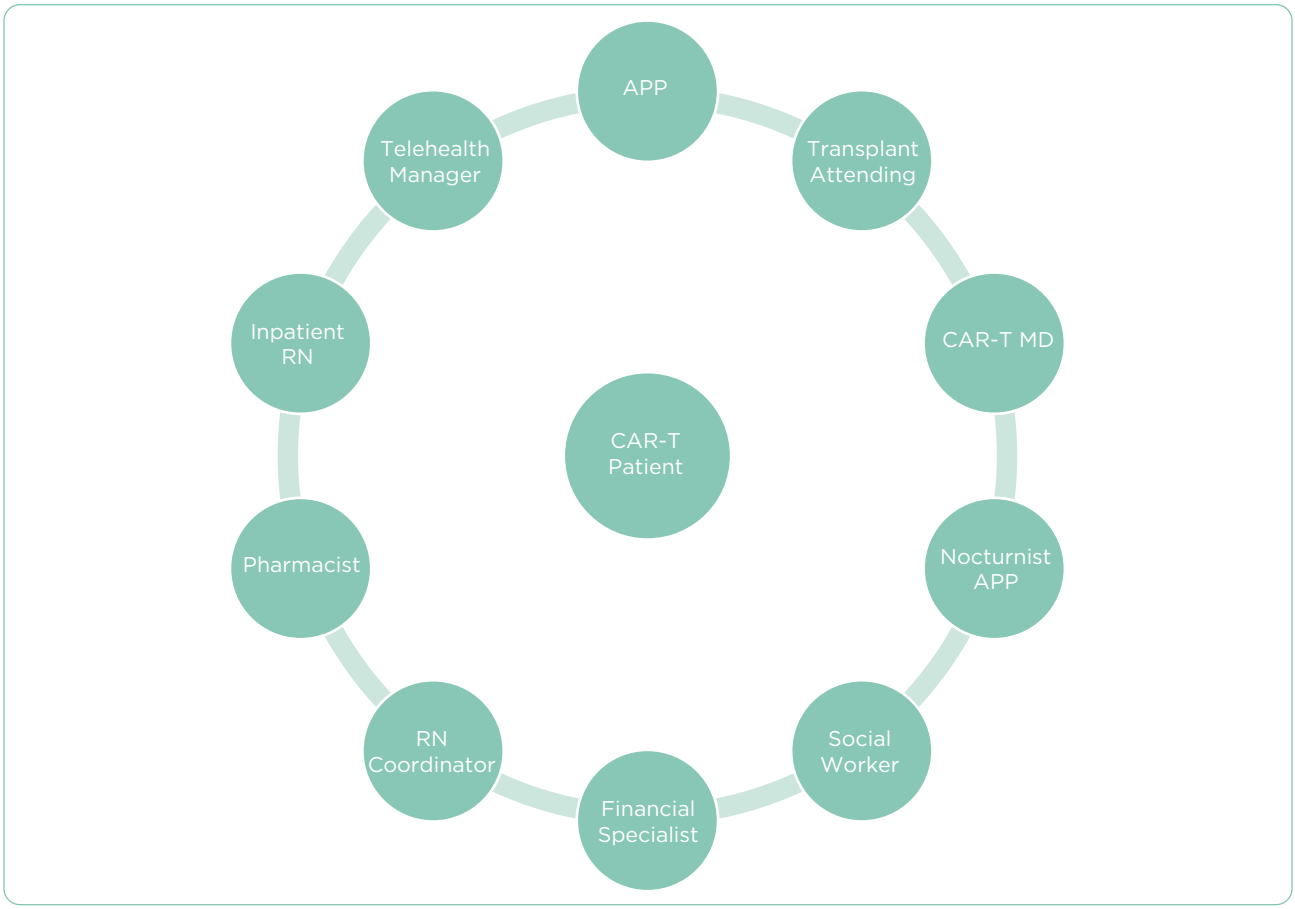

Figure 1. Multidisciplinary team members of the commercial CAR T-cell therapy program.

specialty consults with endocrinology, cardio-oncology, nephrology, and dental procedures. It is imperative for patient safety to manage chemotherapy-induced heart failure, chronic kidney disease, diabetes, hypothyroidism, adrenal insufficiency, and dental caries prior to CAR T-cell infusion. The utilization of specialized APPs in this role allows for physicians to focus on patient recruitment and evaluation for CAR T-cell therapy while allowing APPs to practice at the top of their experience and licensure, providing efficient management of our CAR T-cell therapy program.

On day 0, the CAR-T cells are infused into the patient. The patient is then seen in clinic twice daily. They are seen early in the morning by a physician to evaluate labs, provide necessary treatments, and assess for CRS and neurotoxicity. If the patient is doing well, they are able to go home if they live within 30 miles of the medical facility or to a nearby apartment until late afternoon. The patient then returns to clinic in the late afternoon to be seen by an APP who checks for toxicities and side effects. At this afternoon visit, the patient is seen by the nocturnist APP to establish a baseline prior to their nighttime telemedicine visit. Patients are seen in this cadence—twice daily in clinic and via telemedicine—for the first 14 days following infusion (Figure 2). It has been determined through evaluation of peer-reviewed publications that these first 14 days present the highest risk for severe toxicities and thus is the reason for our determination of this time frame.

The nocturnist APP team performs the telemedicine visits each night. This visit consists of vital signs taken by the patient or caregiver at home using hospital-grade calibrated equipment, extensive review of systems to evaluate for CRS or neurotoxicity, and thorough neurologic exam. This visit is performed over encrypted video conference call, which is incorporated into the EHR system allowing for a consistent, safe, and private visit for the patient and caregiver.

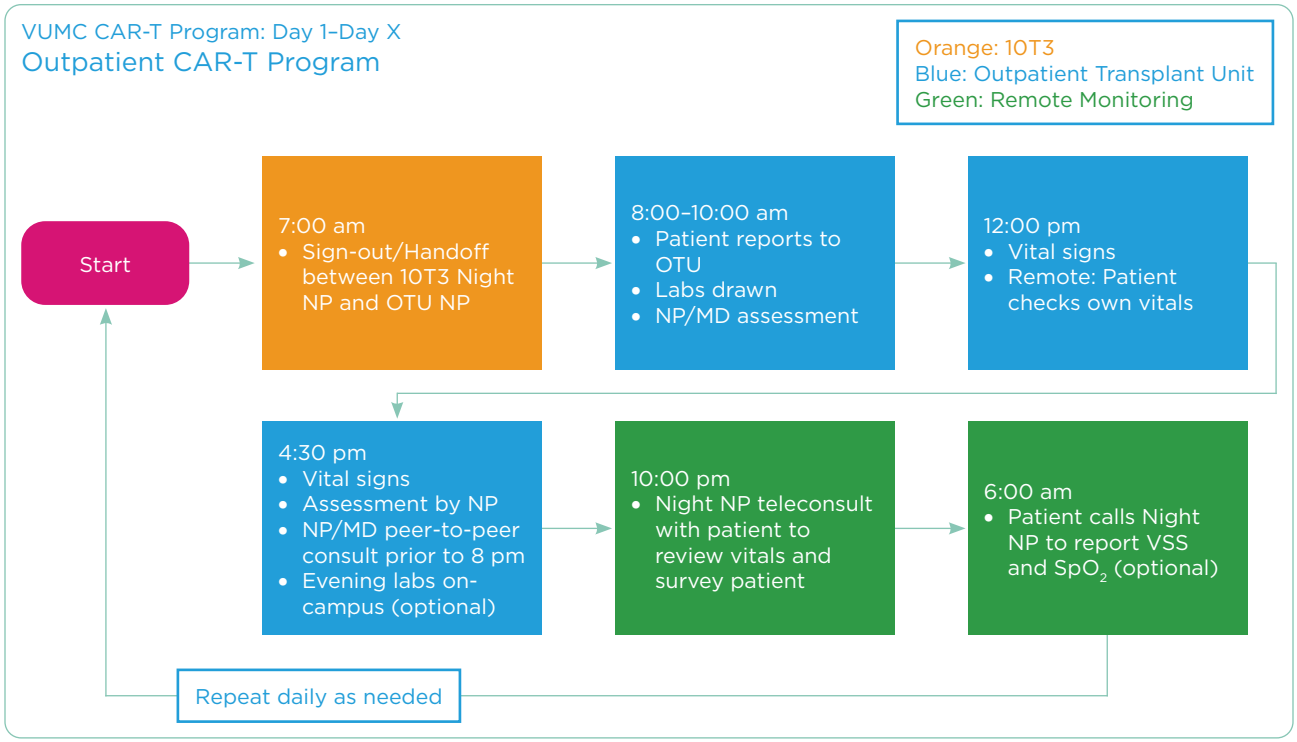

Figure 2. Outpatient CAR-T program. OTU = outpatient transplant unit.

Prior to the start of our outpatient telemedicine CAR T-cell therapy program, admission criteria were decided upon by the physician and APP team. These criteria allowed for safe and consistent decision-making across our provider team regardless of who is on call or performing the telemedicine visit. Our admission criteria include neurologic changes, signs of CRS, neutropenic fever, and signs of sepsis. Additionally, we have utilized a dedicated "Stat bed" for direct admissions to our inpatient unit from home after hours. This allows our CAR T-cell patients to be triaged by the APP and bypass the ED, where exposure to infection or prolonged wait time and delay to treatment is a concern. Once the patient arrives to our specialty unit, they are evaluated in person by the APP who will determine if the patient requires an infectious workup, tocilizumab, or steroids. The APP will consult with the physician on call to determine parameters to initiate treatment or escalate care to the intensive care unit (ICU).

After the initial implementation of the outpatient telemedicine care model, we determined that there was a significant need for training of the ED staff (MDs, APPs [including pharmacists], and RNs) to recognize and quickly treat any possible toxicities of CAR T-cell therapy. One concern the oncology team had with the transition of an inpatient model to the outpatient setting was that a CAR T-cell therapy patient may present to the ED without notifying the APP on service. The development of an ED CAR T-cell pathway helped to standardize patient care outside of our dedicated 24/7 team. We also recognize that CAR T-cell therapy is a relatively new therapy, and it is possible that toxicities may be seen outside of this 14-day close monitoring window. This pathway is constantly being revisited and revised to improve efficiency and quick delivery of treatment. Our ED providers and pharmacists have been Risk Evaluation and Mitigation Strategy (REMS) trained according to CAR T-cell center guidelines.

When a CAR T-cell patient presents to the ED, a banner notification within the EHR system notifies the RN or provider that the patient has had CAR T-cell therapy. Each patient is also given a CAR T-cell wallet card to present to ED staff to notify providers and staff of their CAR T-cell therapy status. Subsequent interventions are based on the patient's presenting symptoms and provider assessment as per the most recent American Society for Transplantation and Cellular Therapy (ASTCT) guidelines for management of toxicities (Lee et al.,

2018). Following recognition of a patient's CAR T-cell status, the ED providers notify the BMT team per hospital triage guidelines. The on-call BMT attending physician notifies the nocturnist in-house APP, who then evaluates the patient.

If CRS is identified, the APP notifies the BMT attending and they discuss the administration of tocilizumab. If it is determined that tocilizumab is to be administered, it is ordered stat and the ED RN is then instructed to call the pharmacy to ensure the tocilizumab arrives at bedside and is administered as soon as possible. If signs of neurotoxicity are present, the BMT attending physician is notified and the determination of oral vs. IV dexamethasone is made based on current guidelines. If there is a concern for sepsis, the ED provider provides a standard sepsis evaluation, resuscitation, and initiation of IV antibiotics (National Comprehensive Cancer Network, 2018). Toxicities are graded based on the ASTCT consensus guidelines. Since sepsis and severe CRS can be difficult to differentiate in an emergency setting, if the patient requires ventilatory or vasopressor support, ED providers have been instructed to administer tocilizumab, and the patient is admitted to the ICU for close monitoring. Throughout the entire ED pathway discussed above, closed and open communication with the APP and CAR T-cell therapy attending is crucial to ensure patient safety and resolution of toxicities.

OPERATIONAL CHALLENGES

There were many operational challenges in the development of an outpatient telemedicine CAR T-cell therapy care model. One of the initial operational challenges was developing proper safety nets for patients. Weekly hour-long multidisciplinary and multidepartmental meetings were held for many months prior to going live with this care model. This group developed standardized eligibility criteria, telemedicine visit templates, admission criteria, ensured the availability of a dedicated open bed on a specialized inpatient unit for direct admission, and developed an ED admission pathway as well as multiple back-up plans should our initial pathways fail.

Another operational challenge was ensuring proper education of staff and patients. Every multidisciplinary member of our team who could possibly provide care for CAR T-cell therapy patients was required to undergo REMS training. This was a large administrative undertaking to identify the physicians, fellows in training, APPs (including pharmacists), RNs, and ED providers who would need to be trained. With the continuous turnover of staff at an academic institution, this continues to be a challenge. This new model also required additional education for APPs on the use of telemedicine services encrypted through our EHR system. In addition to provider education, each patient also requires education on the use of the encrypted telemedicine technology. In this model, each patient receives an individual teaching session in which a practice telemedicine visit is set up and the patient is walked through the process of logging in and participating in the telemedicine visit.

The technology itself was an operational challenge. Given that telemedicine is not typically utilized by inpatient providers, identifying and obtaining technology equipment was a challenge. Close working relationships with the information technology department was essential. An additional challenge is ensuring that the tablet, smartphone, or computer used by the patient was capable of using the encrypted telemedicine software. Reliable internet service is also an ongoing operational challenge. Many patients stay in local short-term housing for the first 30 days following CAR T-cell therapy to ensure close monitoring. These housing options do not always provide high-quality, reliable internet access, which can create a challenge for the video conferencing telemedicine visit.

Ensuring a consistent and reliable 24/7 contact for patients was another operational challenge. We identified the APPs as the most consistent, efficient, and reliable team for patients to contact. To address this challenge, it was determined that the APPs would carry a dedicated "CAR-T" cell phone. This ensures that the outpatient CAR T-cell therapy patients have a direct line of communication at all times in the event they have questions, concerns, or are experiencing any acute symptoms that may warrant hospital admission. Our CAR T-cell patients are all provided with the phone number for the CAR-T phone and are reminded to call this phone first for all inquiries and reports of any concerning events. In case of missed calls, back-up lines of communication for the CAR T-cell pa-

tients include calling the hospital's access center or the dedicated specialty unit directly.

One final operational challenge includes the workflow of our APP team. The team responsible for nightly telehealth assessments is our inpatient nocturnist team. In addition to the telehealth responsibilities, these APPs manage malignant hematology, oncology, stem cell transplant, sickle cell, and hemophilia patients admitted to the hospital. These responsibilities include placing orders for patients, admitting patients from the ED, and responding to medical emergencies. It is feasible that these responsibilities may occur concurrently with the scheduled telehealth visits with our CAR T-cell therapy patients. In the event that the APP is not able to perform the telehealth video call at the previously scheduled time due to emergent events occurring in the hospital, the specialized inpatient nursing staff has been identified as the second line to call the patient. Nursing staff are then to ask the patient if there are any concerns and inform the patient that the telemedicine call will be delayed but will still occur.

FUTURE OPPORTUNITIES

At the time of this publication, six patients have been treated utilizing this model, and two have been admitted with an average length of stay of 1.5 days. While the patient subset may be small, the results of delivering high-quality care in a more patient-centered way may be translated for use with further CAR T-cell therapies, bispecific T-cell engager (BiTE) therapy, and dual anti-CTLA-4 and anti-PD-L1 blockade (DART) therapies. The model began with using only one commercial product; after optimization of our operation, we have been able to expand to include both currently available commercial CAR T-cell therapy products. While these two products have different side effect profiles, the overall risks remain the same. The model outlined in this article has been easily adapted to both products. In addition, we have begun the process of creating models for outpatient telemedicine within the scope of clinical trials. Many of these novel immuno-oncology therapies have similar unique toxicities and high risk for CRS. As we continue to optimize our outpatient telemedicine commercial CAR T-cell program, continued expansion to include these other high-risk treatments may be a possible next step.

As the use of immuno-oncology continues to grow, it is reasonable to expect that telemedicine will be utilized as peer-to-peer consult for patients arriving to EDs with toxicities of these therapies. Some community hospital EDs may not have the specialty knowledge to appropriately address the unique toxicities of CAR T-cell therapy and other immuno-oncology therapies. The use of telemedicine to assess and triage patients, similar to telestroke protocols, could feasibly be used to assess and treat our oncology patients in the future, thus expanding access of these therapies to communities and patients who do not have immediate access to a large academic institution.

Continuing to utilize APPs to their full scope of practice to help drive innovative care delivery models will be crucial in this next decade of healthcare delivery. As new treatment modalities arise, APPs are well poised to lead in this area.

CONCLUSION

The multidisciplinary and multidepartmental approach has been critical to the success of the transition of an inpatient CAR T-cell program to the outpatient setting. This has allowed for positive patient experience while maintaining an exceptionally high level of care and safety of CAR T-cell therapy delivery to the patient. The utilization of a specialized team of physicians and APPs allowed for high-level, efficient communication when toxicities arose and swift treatment for patients.

The future is bright for APPs in oncology care. The educational model of physician assistants and nurse practitioners allows their role to continue to grow and develop as new treatments continue to improve. Advanced practice providers have been shown to provide efficient, high-quality, and cost-effective care. Examples of cost-effective outcomes as a result of the utilization of APPs include decreased length of stays and hospital admissions (Newhouse et al., 2011). As reimbursement moves further towards the Oncology Care Model, APPs will prove to be beneficial to employ in the treatment of oncology patients. Advanced practice providers have the knowledge base and education to understand a broad range of disease processes, implement diverse treatment modalities, and effectively manage the unique toxicities associated with these specialized treatments.

Disclosure

The authors have no conflicts of interest to disclose.

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