



# Changing the Tune for CAR T-Cell Therapy

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**A Music City Experience in  
Remote Patient Monitoring**

Though remote patient monitoring platforms have been used effectively throughout the COVID-19 pandemic to reduce the burden on patients and healthcare facilities around the country, Vanderbilt University Medical Center, Vanderbilt-Ingram Cancer Center, Nashville, Tenn., has been using this technology in a different capacity—with its patients who are being treated with chimeric antigen receptor (CAR) T-cell therapy. Today, these patients are monitored 24/7 via remote technology, alerting cancer program staff to any significant changes in clinical status that would initiate a hospital admission.

### CAR T-Cell Therapy Adverse Events

In 2017, the U.S. Food and Drug Administration (FDA) approved the first CAR T-cell therapy for patients with diffuse large B-cell lymphoma.<sup>1</sup> Today these therapies are also approved for follicular lymphoma, mantle cell lymphoma, acute lymphoblastic leukemia, and multiple myeloma, yet this treatment comes with significant side effects.<sup>1-5</sup>

Patients who undergo CAR T-cell therapy experience toxicities when these modified T-cells bind and become activated, releasing inflammatory cytokines. Cytokine release syndrome can present as fever, hypotension, tachycardia (a heart rate of more than 100 beats a minute), and/or hypoxia (low oxygen in the tissues). Initially, providers treat these side effects symptomatically with acetaminophen, intravenous fluids, and other medications. If symptoms do not dissipate or if symptoms escalate, tocilizumab is indicated per American Society of Transplant and Cell Therapy guidelines published in 2019.<sup>6,7</sup> Corticosteroids can also be used if the cytokine release syndrome is refractory to tocilizumab.<sup>6,7</sup>

The second main adverse event that is seen with patients who are receiving CAR T-cell therapy is called immune effector cell-associated neurological syndrome. This syndrome can present through a variety of symptoms, including tremors, confusion, aphasia (loss of the ability to understand or express speech), or

even seizures. The American Society of Transplant and Cell Therapy recommends performing a neurological assessment called the “ICE score” every shift (every 12 hours) on these patients to assess their neurological status and ensure that no significant changes have occurred. If neurological changes are noted, corticosteroids should be initiated.<sup>6,7</sup> Table 1, page 22, shows the incidence of cytokine release syndrome and immune effector cell-associated neurological syndrome for each CAR T-cell therapy product that was FDA-approved as of June 27, 2022.

### Implementing Remote Patient Monitoring

Traditionally, patients being treated with CAR T-cell therapies require a hospital admission to manage their toxicities. To avoid these hospitalizations during the COVID-19 pandemic, Vanderbilt-Ingram Cancer Center developed and implemented a remote patient monitoring and telehealth model that allowed patients to be safely treated in the outpatient clinic setting. Developing this model took buy-in from many different players, including physicians, advanced practice practitioners (APPs), nursing, administrators, and patients. With nocturnist APPs performing nightly telehealth visits at 10:00 PM, no additional staff were needed prior to program implementation.

So how does the model work? At the initiation of a CAR T-cell therapy, all patients receive the remote monitoring device. Though the technology is provided at no additional cost, patients must sign a consent form saying that they will return the device and all associated equipment at treatment completion or they may be charged for the cost of the technology. The patient care coordinator educates patients and caregivers on how to use the technology by practicing hands-on with the device and troubleshooting possible issues that may occur. A pre- and post-test to measure competency and knowledge about taking vital signs with the monitoring device ensures that patients' caregivers fully understand how to use the technology.

Patients are then seen daily in the outpatient clinic. After their in-person morning clinic appointment, patients check in with providers virtually at multiple touchpoints (see Figure 1, right). With this telehealth model, clinicians monitor vital signs and can

quickly intervene as clinically indicated. Patient care coordinators and APPs monitor patients' vital signs during the day and after-hours; as mentioned earlier, the nocturnist APP monitors patients' vital signs throughout the night. The remote monitoring system automatically generates alerts—via a mobile app and email—about any medical issues patients experience.

Remote monitoring of patients being treated with CAR T-cell therapies allows these patients to be treated safely in the outpatient setting, while the technology enables providers to watch for subtle clinical signs that would indicate a potential presentation of toxicity. This early identification allows for early intervention. In turn, early intervention has been shown to reduce toxicity burden on patients. For example, if the clinical team notes an increasing body temperature while patients are at home (or at local lodging if they must travel for treatment), providers can communicate immediately with patients and initiate appropriate intervention(s).

**Table 1. Incidence of Adverse Events in Patients on CAR T-Cell Therapies<sup>2-5,8-12</sup>**

Therapy	Indication(s)	Clinical Trial	Cytokine Release Syndrome Incidence	Immune Effector Cell-Associated Neurological Syndrome Incidence
Tisagenlecleucel (Kymriah <sup>®</sup> )	Relapsed/refractory diffuse large B-cell lymphoma or acute lymphoblastic leukemia in patients 25 years and younger	JULIET (NCT02445248)	93	64
Axicabtagene ciloleucel (Yescarta <sup>®</sup> )	Relapsed/refractory diffuse large B-cell lymphoma or follicular lymphoma	ZUMA-1 (NCT02348216) ZUMA-5 (NCT03105336)	93 (diffuse large B-cell lymphoma); 84 (follicular lymphoma)	64 (diffuse large B-cell lymphoma); 77 (follicular lymphoma)
Brexucabtagene autoleucel (Tecartus <sup>®</sup> )	Relapsed/refractory mantle cell lymphoma or relapsed/refractory acute lymphoblastic leukemia in patients 18 years and older	ZUMA-2 (NCT02601313) ZUMA-3 (NCT02614066)	91 (mantle cell lymphoma); 92 (acute lymphoblastic leukemia)	81 (mantle cell lymphoma); 87 (acute lymphoblastic leukemia)
Lisocabtagene maraleucel (Breyanzi <sup>®</sup> )	Relapsed/refractory diffuse large B-cell lymphoma	TRANSCEND (NCT02631044)	46	35
Idecabtagene vicleucel (Abecma <sup>®</sup> )	Relapsed/refractory multiple myeloma	KarMMa (NCT03361748)	84	18
Ciltacabtagene autoleucel (Carvykti <sup>™</sup> )	Relapsed/refractory multiple myeloma	CARTITUDE-1 (NCT03548207)	95	23

Another benefit: the outpatient CAR T-cell therapy remote monitoring program allows inpatient units greater bandwidth to care for the general oncology population. In a traditional care delivery model, patients on CAR T-cell therapies are admitted to the hospital for up to 14 days to monitor for cytokine release syndrome and immune effector cell-associated neurological syndrome. Transitioning these patients to remote monitoring in the outpatient clinic setting frees up inpatient beds for acutely ill patients.

Finally, treating these patients in the outpatient clinic setting versus the more expensive inpatient setting provides significant cost savings to patients, the hospital, and healthcare system.

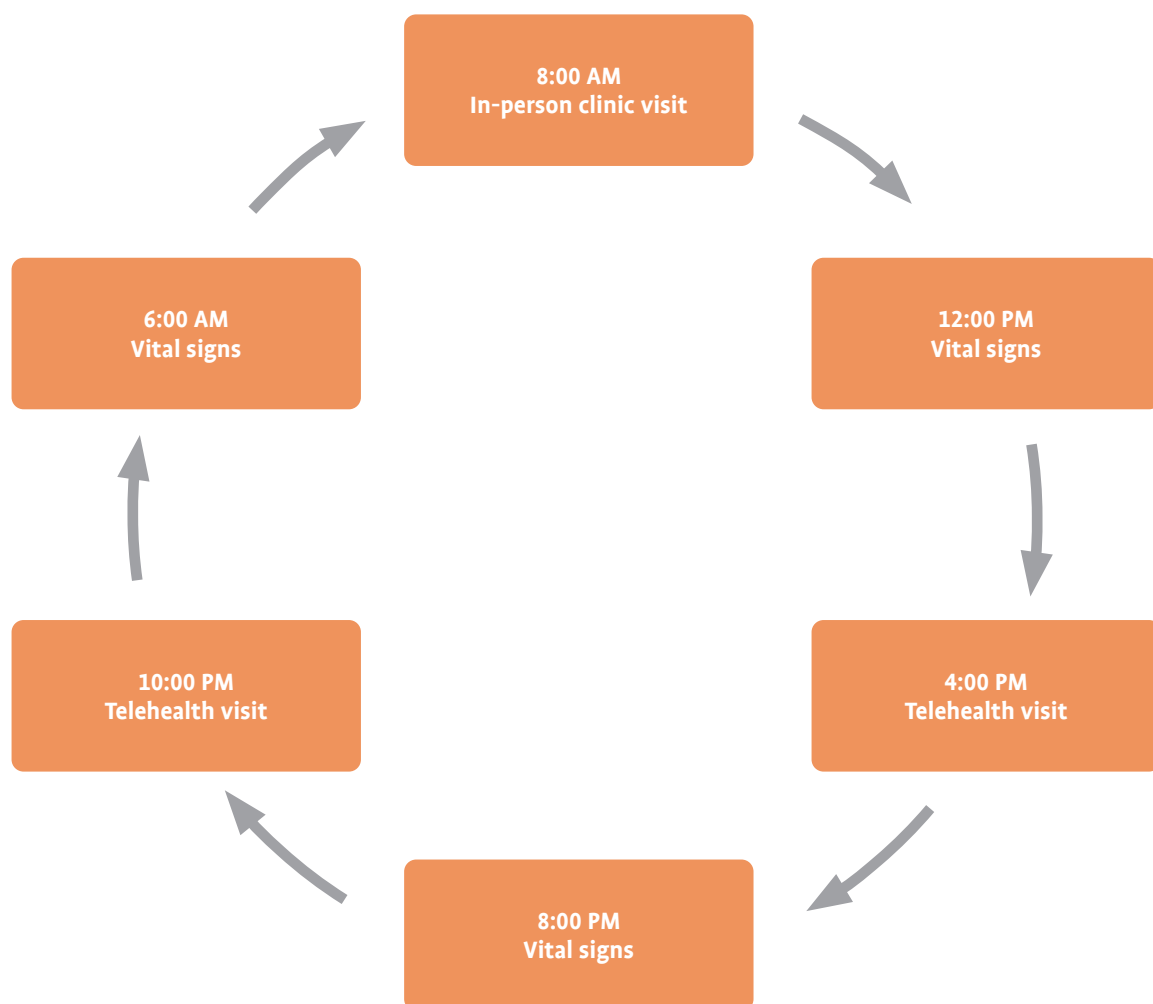
### Improving the Patient Experience

Not only is remote monitoring of patients on CAR T-cell therapies safe and effective for them and their caregivers, but Vanderbilt-Ingram Cancer Center has found that this model of care delivery

improves the overall patient experience. Patients remain in the comfort of their homes or local lodging with their caregivers, avoiding a prolonged hospitalization marred by ringing alarms, lack of privacy, and ongoing COVID-19 safety concerns.

The remote patient monitoring platform is both patient- and clinician-friendly and has not placed a large burden on patients, caregivers, clinicians, or staff. The vital signs automatically load into the dashboard in 15-minute increments from an armband that patients wear with a device that tracks pulse oximetry, heart rate, respiratory rate, and temperature in real time. Patients and/or their caregivers have to place and activate a blood pressure cuff to input this metric, but after their blood pressure is taken, the value is pushed to the dashboard for healthcare providers to view. The healthcare provider is responsible for viewing patients' vitals and assessing whether any are out of the normal range, which may warrant hospital admission or some other intervention.

Figure 1. Daily Schedule of Patients on Remote Patient Monitoring



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## The use of remote monitoring for patients undergoing CAR T-cell therapy allows the cancer care team to note subtle clinical changes that would potentially go unnoticed until a scheduled clinical touchpoint.

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Patient compliance has been very high because patients want to stay out of the hospital as much as possible. Because CAR T-cell therapy treatment is already a large stressor, it was important that this technology not add another layer of stress to patients and caregivers. Instead, patients have expressed increased security because they are being monitored around the clock.

### Improving Toxicity and Side Effect Management


The use of remote monitoring for patients undergoing CAR T-cell therapy allows the cancer care team to note subtle clinical changes that would potentially go unnoticed until a scheduled clinical touchpoint. For example, during the night, remote patient monitoring technology may alert providers that a patient's oxygen levels are decreasing. All vital signs are pushed to the dashboard without the patient having to manually enter the data into the portal. This reduces the burden on patients, caregivers, and cancer program staff. The technology also reduces the risk of human error during input. Providers can call the patient immediately and assess the need for intervention in real time. Without this technology, providers would not yet know about this clinical change until a scheduled vital sign check.

Vanderbilt-Ingram Cancer Center has also implemented a standard operating procedure that allows providers to differentiate patients who need to be admitted for fever and those who can be treated as an outpatient for their cytokine release syndrome.

### Financial Impact on the Cancer Program

As the use of CAR T-cell therapies continue to expand in the outpatient setting, providers have found it difficult to navigate the financial components of this costly treatment. Developing an effective billing model has been greatly challenged by the lag in payers recognizing CAR T-cell therapy as standard of care. Most payers still treat it as experimental and follow Medicare guidelines for payment.

When patients being treated with CAR T-cell therapies are admitted as inpatients within 72 hours of infusion, Vanderbilt-Ingram Cancer Center is impacted financially by inadequate reimbursement. Preventing those inpatient admissions is not only

better for patients, but it also helps protect the financial viability of the cancer program. Adoption of remote patient monitoring technology will inform providers about the slightest changes in patients' vital signs, allowing patients to be brought into the outpatient clinic for evaluation and supportive care versus receiving those services in the more costly inpatient setting. 

*Brittney M. Baer, BSN, RN, is a patient care nurse coordinator for the Immune Effector Cell Program, and Nancy C. Long, MSN, AGACNP-BC, is a nurse practitioner and team lead in the Hematology-Oncology/Stem Cell Transplant and Cellular Therapy Department at Vanderbilt University Medical Center, Vanderbilt-Ingram Cancer Center, Nashville, Tenn.*

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