# Inpatient cancer rehabilitation in a CAR T-cell therapy lymphoma patient with CRS and CRES toxicity

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## INTRODUCTION

Cellular immunity using T-cells' chimeric antigen receptors and their cytotoxic specificity against tumor cells (CAR T-cell therapy) is a new and emerging treatment for a number of cancers. Cytokine Release Syndrome (CRS) and CAR T-cell related Encephalopathy Syndrome (CRES) are common toxicities and can cause significant medical and functional morbidity.

Although not previously documented in CAR T-cell treated cancer patients, acute inpatient cancer rehabilitation has been shown to be effective in patients with neutropenic and thrombocytopenic precautions, requiring frequent transfusion support, and with significant neurologic deficits. FIM improvements in a number of cancer patient populations have also been documented with acute inpatient rehabilitation.

**Chimeric Antigen Receptor (CAR) Cell Therapy Toxicity Assessment and Management - Adult**

*This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson's specific patient population; MD Anderson's services and structure; and MD Anderson's clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. The algorithm should not be used to treat pregnant women.*

APPENDIX C: Grading of CRS (Note: CRS grade should be determined at least twice daily and any time there is a change in patient's status)

| Category | Sign/Symptom | CRS Grade 1[1] | CRS Grade2[2] | CRS Grade 3[2] | CRS Grade 4[2] |
|---|---|---|---|---|---|
| Vital signs | Temperature greater than or equal to 38° C | Yes | Any | Any | Any |
| | SBP less than 90 mmHg | No | Responds to N fluids or low-dose vasopressor | Requires high-dose or multiple vasopressors[3] | Life-threatening |
| | Needing oxygen to maintain $0_2$ saturation greater than 90% | No | $FiO_2$ less than 40% | $FiO_2$ greater than or equal to 40% and/or requiring BiPAP | Requires ventilator support |
| Organ Toxicity | See Appendix E | Grade 1 | Grade 2 | Grade 3 or grade 4 transaminitis | Grade 4 except grade 4 transaminitis |

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APPENDIX E: Grading of CRES

| Symptom/Sign | Grade 1 | Grade2 | Grade3 | Grade4 |
|---|---|---|---|---|
| Neurological assessment score (see below) | Mild (7-9) | Moderate (3-6) | Severe (0-2) | Critical / obtunded |
| Raised intracranial pressure | - | - | Stage 1 or 2 papilledema[1] with CSF opening pressure less than 20 mmHg | Stage 3, 4, or 5 papilledema[1] or CSF opening pressure greater than or equal to 20 mmHg or cerebral edema |
| Seizures or motor weaknesses | - | - | Partial seizure or non-convulsive seizures on EEG responding to benzodiazepine | Generalized seizures or convulsive or non-convulsive status epilepticus or new motor weakness |

CARTOX 10-point neurological assessment
(Assign one point for each task performed correctly; score of 10 = normal)
- Orientation to year, month, city, hospital, President: 5 points
- Name 3 objects (point to clock, pen, button): 3 points
- Ability to write a standard sentence (e.g., Our national bird is the bald eagle): 1 point
- Count backwards from 100 by ten: 1 point

FIM Transfers/Locomotion Level

7 Complete independence
6 Modified independence: Requires use of a device but no physical help
5 Supervision: Requires only standby assistance or help with set-up
4 Minimal assistance: Requires incidental help (subject performs > 75% of the task)
3 Moderate assistance: Subject performs 50–75% of the task
2 Maximal assistance: Subject provides less than half of the effort (25–49%)
1 Total assistance Subject contributes < 25% of the effort or is unable to do the task

## OBJECTIVE

To describe the inpatient course including inpatient rehabilitation of a lymphoma patient status post CAR T-cell therapy with CRS and CRES toxicities.

## CASE DETAILS

75-year-old gentleman with diffuse refractory large B-cell lymphoma status post multiple treatments who presented to our institution for CAR T-cell therapy. Prior to hospital admission the patient underwent outpatient CAR-T cell apheresis followed by lymphodepletion therapy w/ fludarabine and cyclophosphamide. He then received inpatient CAR-T cell infusion therapy on Day 1.

The patient's social history was retired, married and had flown to Houston by commercial airline. He and family were staying in a local hotel with elevator access and ground transportation shuttle. Their own home is 2 stories with full bathroom upstairs. Wife has a history of back issues and cannot provide significant physical assistance. The patient and family have resources to hire additional caregiver help if necessary.

Past Medical History pertinent for hypertension and CAD. Past Surgical History pertinent for bilateral knee arthroplasty and cardiac stent placement.

Labs WBC 2.4 Hgb 9.3 Platelet 21 Calcium 7.8 Ferritin 8440 CRP 4.23 Bilirubin 1.7

FIM Transfers Mod Assist FIM Locomotion Min assist with RW 75 ft.

Physical Exam
Gen. well-developed tall cachectic gentleman in no acute distress
Sleepy but arousable.
Abdomen soft distended nontender to palpation
Heart exam S1-S2
2+ pedal edema
4 minus out of 5 strength proximally and distally in the upper extremities
3 minus out of 5 strength proximally and distally in the lower extremities
Follows commands

PMR impression was that the patient had significant deconditioning, fatigue, impaired cognition, impaired mobility and impaired self-care and would benefit from additional physical occupational and speech pathology treatments with goals of min assist to supervision with mobility and self-care. The patient could not currently tolerate acute inpatient rehabilitation unit intensity of rehabilitation therapies. Recommendations were to increase tolerance and participation in rehabilitation therapies, maintain fall precautions at all times and maximize nutritional status.

From Day 14- Day 26 the patient's medical status, tolerance to rehab therapies and functional status improved. The patient came off of telemetry on Day 16.

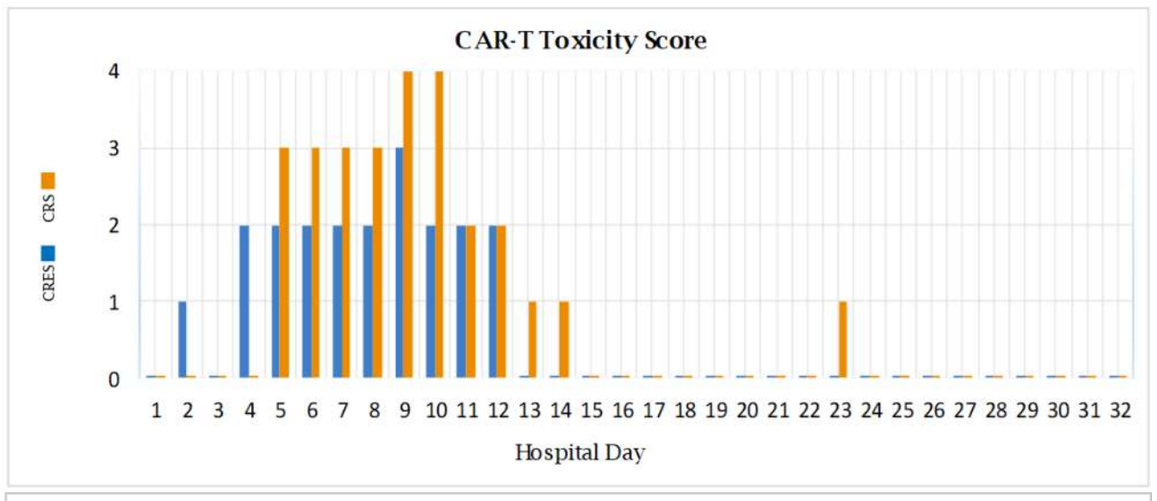
He was transferred to the inpatient rehabilitation unit (IRU) on hospital Day 27. At that time he required min assist with transfers and ambulated 200 ft with min assist.

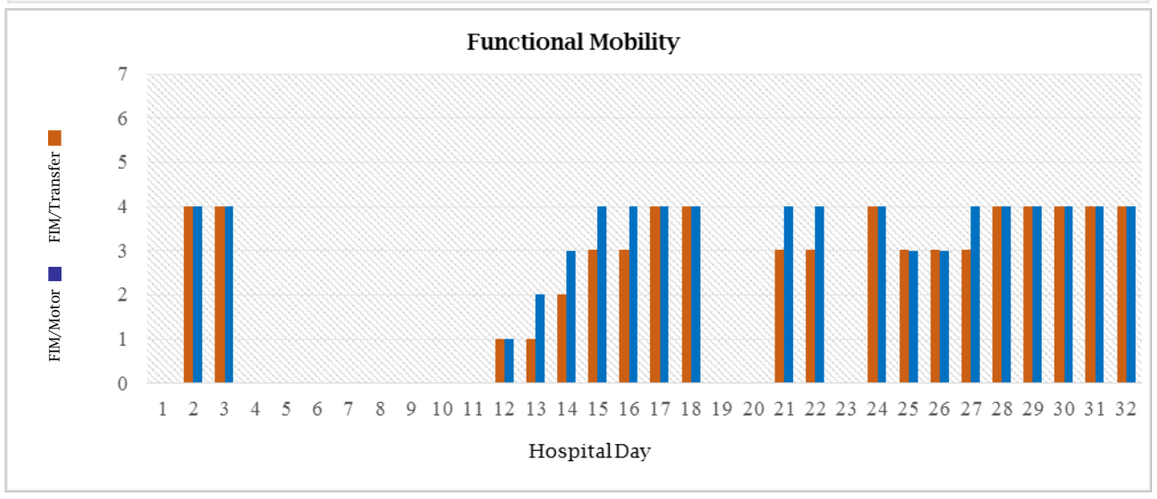
On the IRU the patient required platelet transfusions 4 of 7 days and PRBC transfusion 3 of 7 days secondary to pancytopenia. Additional lab studies which required ongoing monitoring due to CRS included ferritin, CRP, and bilirubin. The patient was continued on Keppra for CRES related seizure prophylaxis and Metoprolol for CRS related ventricular tachycardia.

The patient improved with rehabilitation efforts and was able to transfer and ambulate less than household distances with min assist and go up and down 4 steps with min assist at discharge (Day 32.)

## RESULTS

From initial hospitalization and CAR-T infusion until discharge from our IRU the patient's CRS score improved from 3 (ICU) to 0 (IRU,) CRES score improved from 4 (ICU) to 0 (IRU) and ambulation improved from requiring total assistance (ICU) to requiring less than 25% assistance from another person for less than household distances (IRU.)




## CONCLUSION

A CAR T-cell therapy lymphoma patient who developed significant CRS and CRES toxicities was managed with medical and symptom management and cancer specialized acute inpatient rehabilitation and then safely discharged to the home setting.

Additional experience in recognizing and managing CAR T-cell related toxicities and their functional implications may be important as more patients are treated with this type of immunotherapy. Acute inpatient cancer rehabilitation may be an important option in successful discharge planning for this unique patient population.

## REFERENCES

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