Late Effects and Quality of Life after CAR T-cell Therapy

Hosted by BMT InfoNet

December 18th, 2024

P. Connor Johnson MD
Massachusetts General Hospital

Many thanks to Bristol Myers Squibb whose support helped make this presentation possible.

BMTinfonet.org 30 YEARS EMPOWERING PATIENTS

Late Effects and Quality of Life after CAR T-cell Therapy

P. Connor Johnson, MD
Assistant Professor of Medicine
Massachusetts General Hospital
Harvard Medical School

MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER

CORE
CANCER OUTCOMES RESEARCH & EDUCATION

P. Connor Johnson, MD

Dr. Connor Johnson is an Assistant Professor of Medicine at Harvard Medical School and an attending oncologist at Massachusetts General Hospital. He specializes in cellular therapies such as CAR T-cell therapy and the treatment of patients with lymphoma.

Dr. Johnson's research focuses on addressing the supportive care needs and mitigating the therapy toxicity of patients with lymphoma and patients receiving cellular therapy.

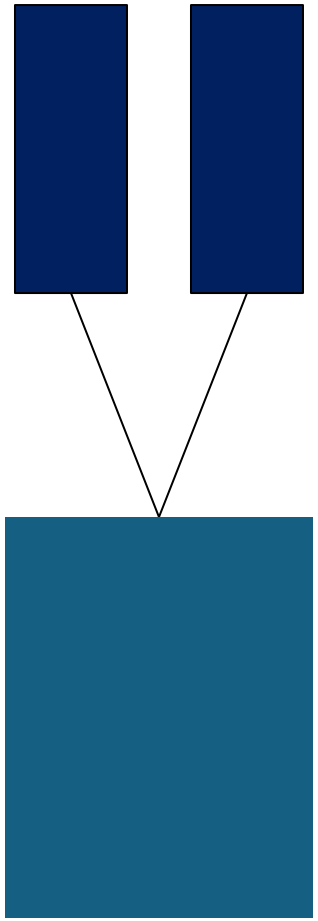
Outline

- The basics of CAR-T cell Therapy
- The patient journey during CAR-T cell therapy
- Psychosocial experience of patients undergoing CAR-T cell therapy
- CAR-T Cell therapy: living with immense prognostic uncertainty
- Early recovery and long-term effects after CAR-T cell Therapy
- Survivorship and beyond

CAR-T Overview

- Chimeric antigen receptor (CAR)-T cell therapy:
  - A form of immunotherapy that uses the cells of the immune system to treat cancer
- 6 FDA-approved products to treat lymphomas, leukemias, and multiple myeloma
- > 100 clinical trials in both solid and blood cancers

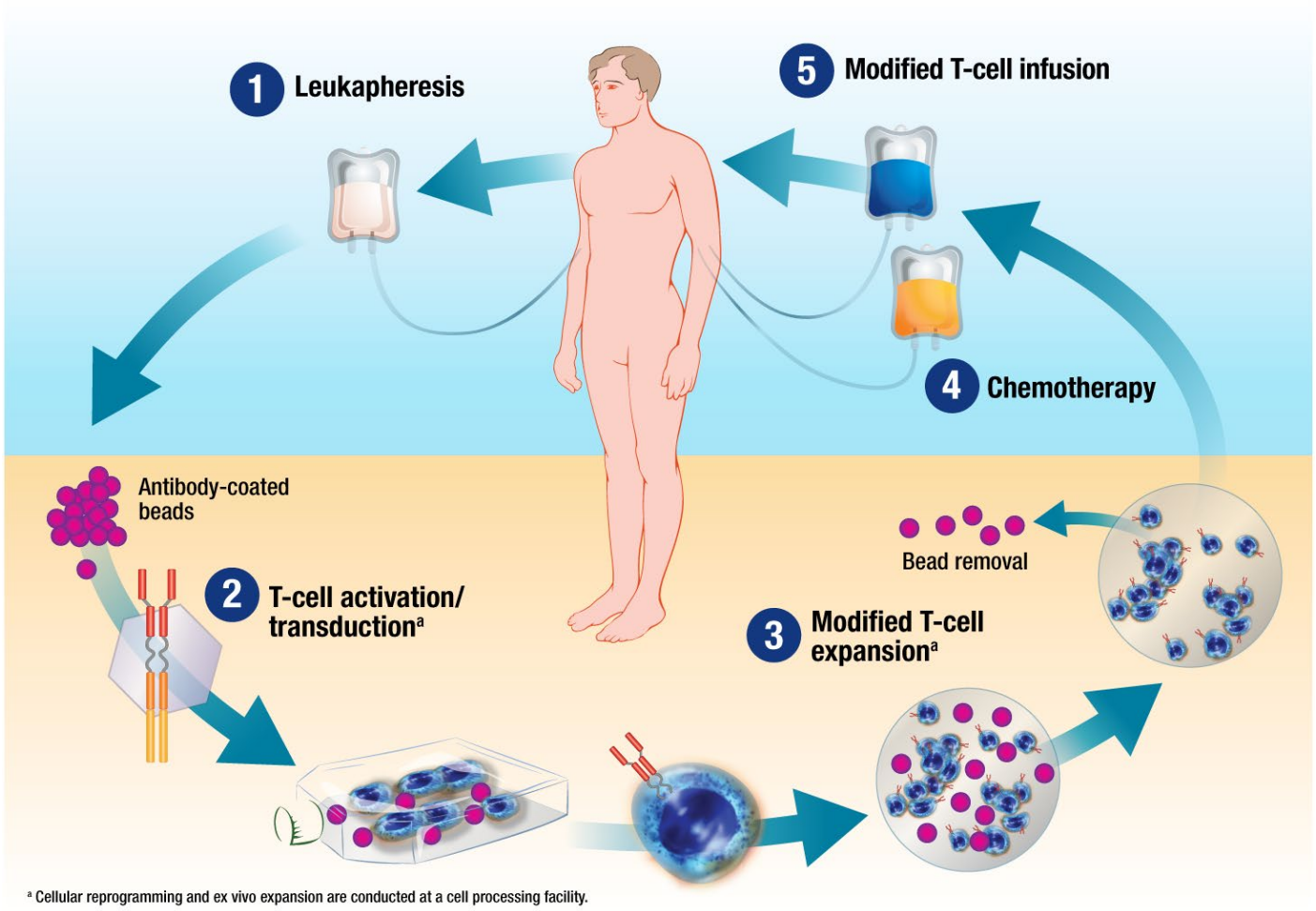
Chimeric antigen receptor (CAR)



Genetically engineered antigen-binding domain (like a latch to bind cancer cells)

Normal T-cell

CAR-T Overview



Courtesy of Marcela Maus

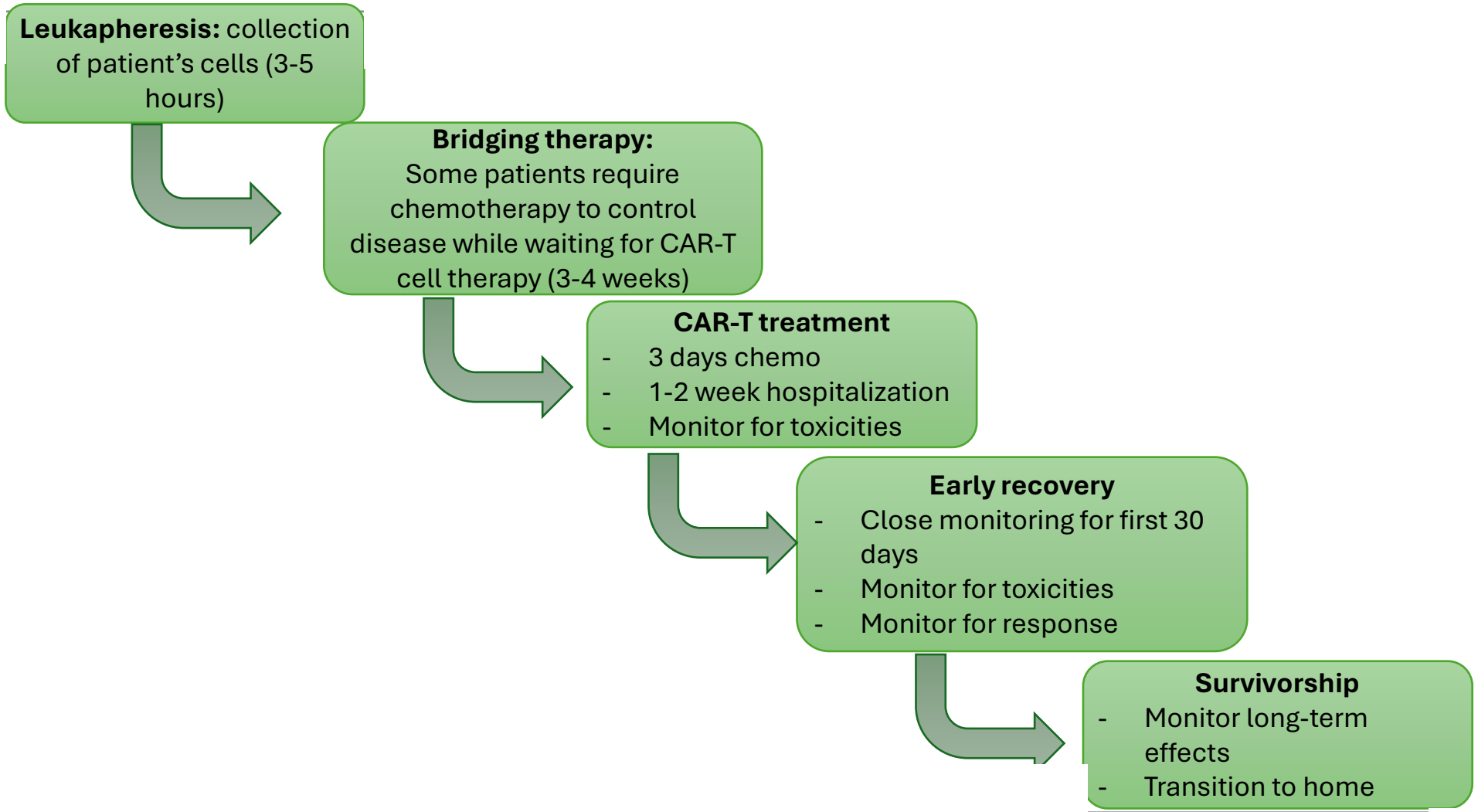
CAR-T Overview

- CAR-T cell therapy is currently approved to treat patients with relapsed/refractory blood cancers such as lymphoma, chronic lymphocytic leukemia and multiple myeloma

- Aggressive lymphomas: often eligible after 1 or 2 prior treatments

- Indolent lymphomas, leukemias, and multiple myeloma: usually eligible after multiple prior treatments

Patient Journey



CAR-T Toxicities

Symptoms of Cytokine Release Syndrome (CRS)	
Fever	Low oxygen
Chills	Low blood pressure
Muscle aches	Joint aches
Fatigue	Headache
Loss of appetite	Organ injury

CAR-T Toxicities

Symptoms of Neurologic Toxicity	
Confusion	Somnolence
Trouble with speech or language	Agitation
Trouble with writing	Seizure
Tremors	Brain swelling

Other CAR-T Toxicities

- Low blood counts
- Low immunoglobulin levels
- Infections
- Immune effector cell-associated hemophagocytic syndrome (IEC-HS) (rare)
- Second cancers (rare)
- Movement and neurocognitive treatment-emergent adverse events (MNTs)

Lange et al. Cancer Med, 2019; Lange et al. Ann Oncol, 2019; Basinski et al. BBMT, 2010; Hoogland et al. Brain Behav Immun, 2019

IEC-HS

- Hyperinflammatory syndrome that typically occurs after cytokine release syndrome has resolved
- Not well understood, but immune cells (T-cells and macrophages) become overactivated
- Abnormalities in coagulation (ability of blood to clot), low blood counts, very elevated ferritin (lab test), and inflammation in the liver are common features
- Disease burden and CAR T-cell product are some risk factors
- Rare, occurring in 1-3% of patients
- Usually managed with anakinra (anti-inflammatory medication) and steroids

Hines et al, 2023; Rajeski et al 2023

Symptoms during CAR-T

Disease Symptoms	Moderate to Severe
Pain	42.9%
Difficulty swallowing	14.3%
Cough	9.5%
Shortness of breath	9.5%
Neuropathy	4.8%
Abdominal bloating	4.8%
Itching	4.8%
Light-headedness	4.8%

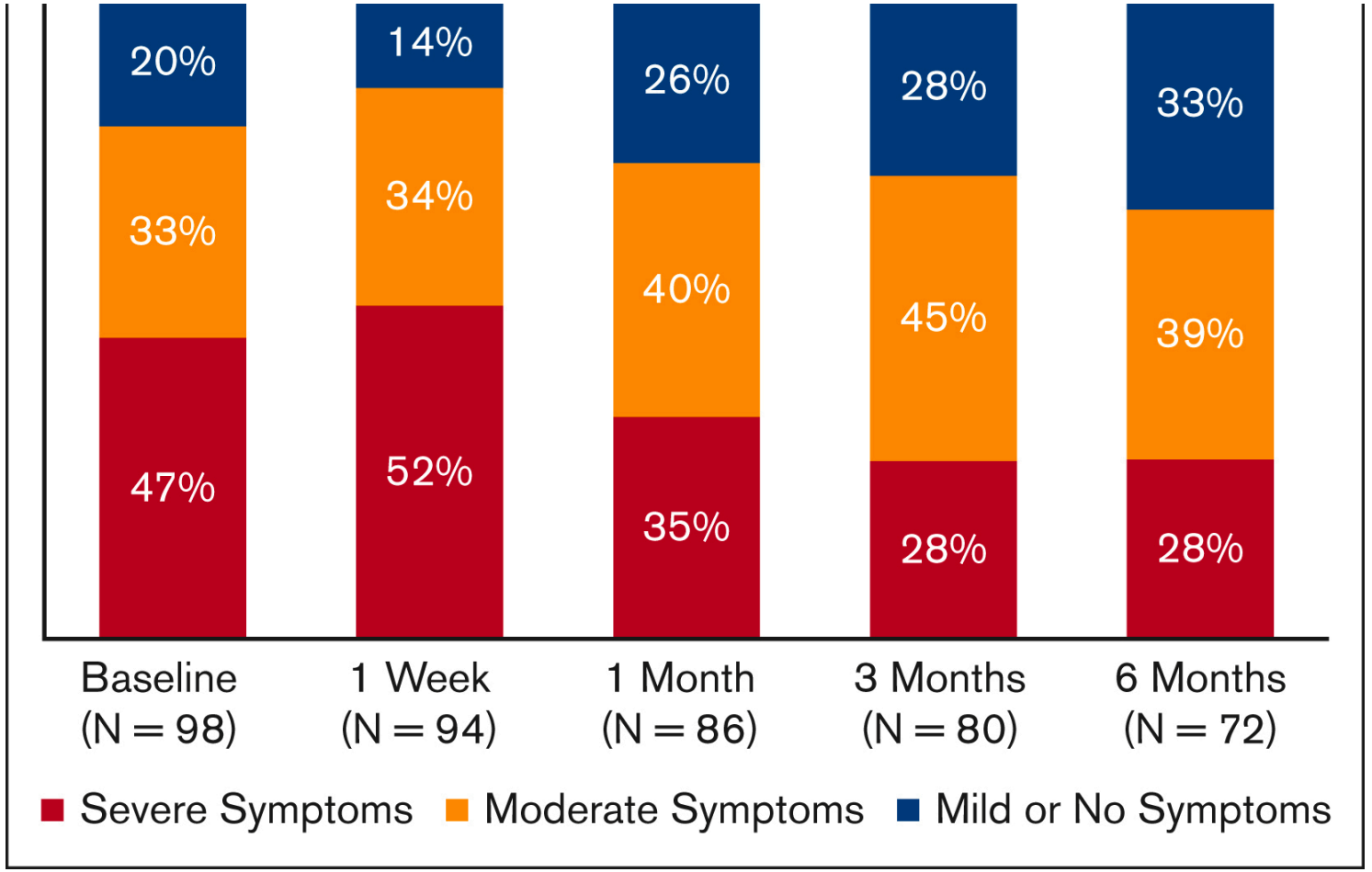
Whisenant, et al. Seminars in Oncology Nursing 2021

Symptoms during CAR-T

CAR-T Symptoms	Moderate to Severe
Fatigue	61.9%
Lack of appetite	28.6%
Headache	28.6%
Chills	28.6%
Feeling confused	23.8%
Memory loss	14.3%
Pain	9.5%
Vomiting	9.5%
Light-headedness	9.5%
Diarrhea	9.5%

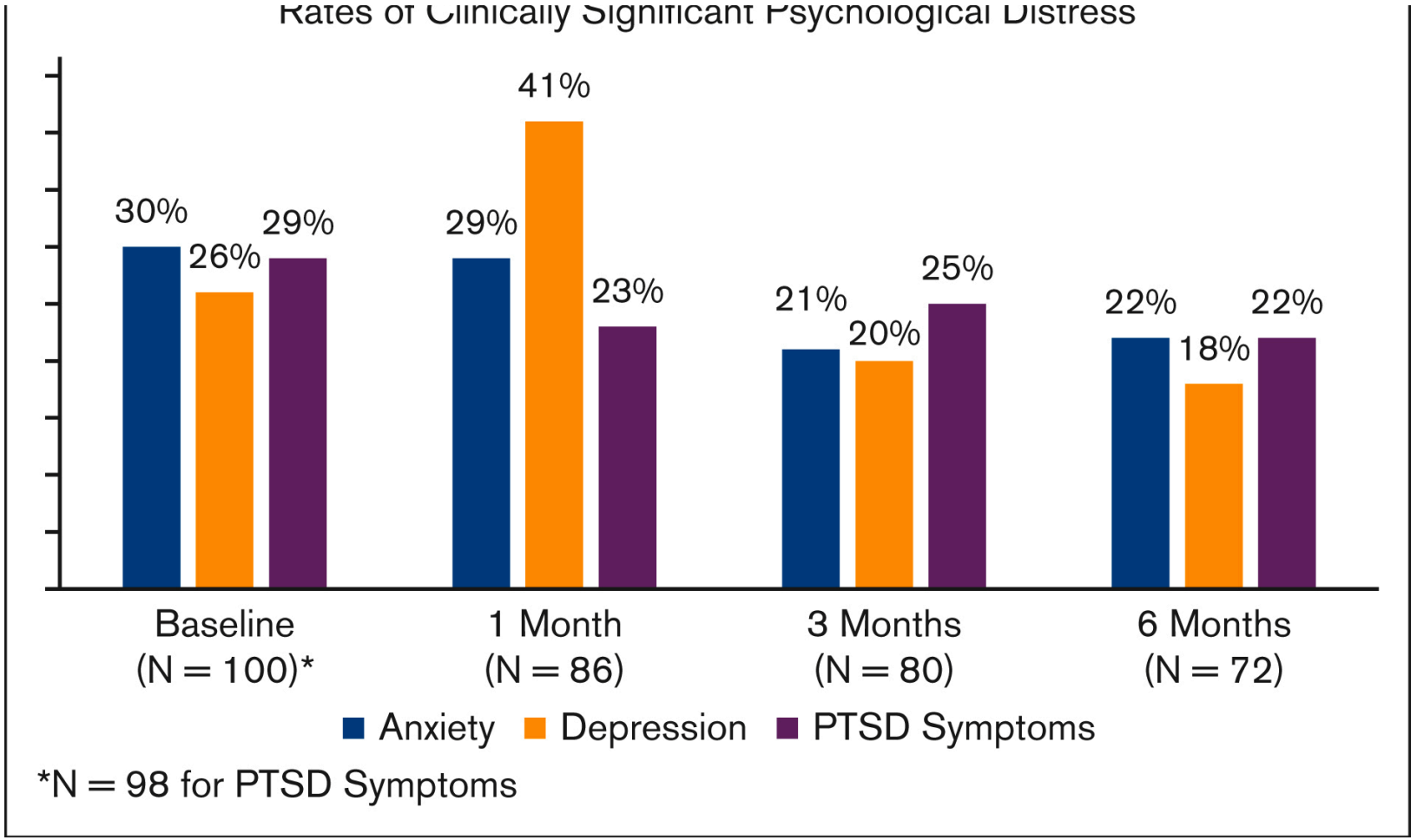
Whisenant, et al. Seminars in Oncology Nursing 2021

Physical Symptoms During CAR-T



Johnson, et al. Blood Adv. 2023.

Psychological Symptoms Over Time



Johnson, et al. Blood Adv. 2023

Prognostic Uncertainty

- Increase in prognostic uncertainty in oncology with novel therapies, especially CAR-T cell therapy

- How to focus on living well and acknowledge risks?

You can't do anything. You can't plan anything, so you never know how long you are going to live. You might live another 20 years. It might be cured, but still the level of uncertainty is painful

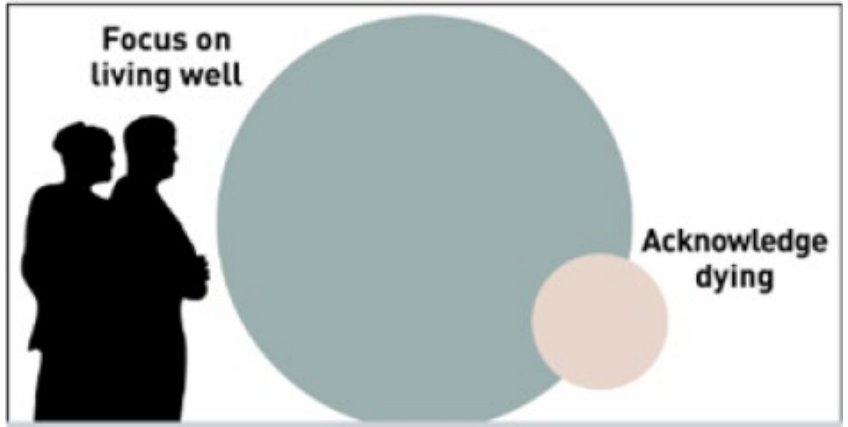


Figure 1d. We stand with the patient and gaze out at the horizon of this frame together.

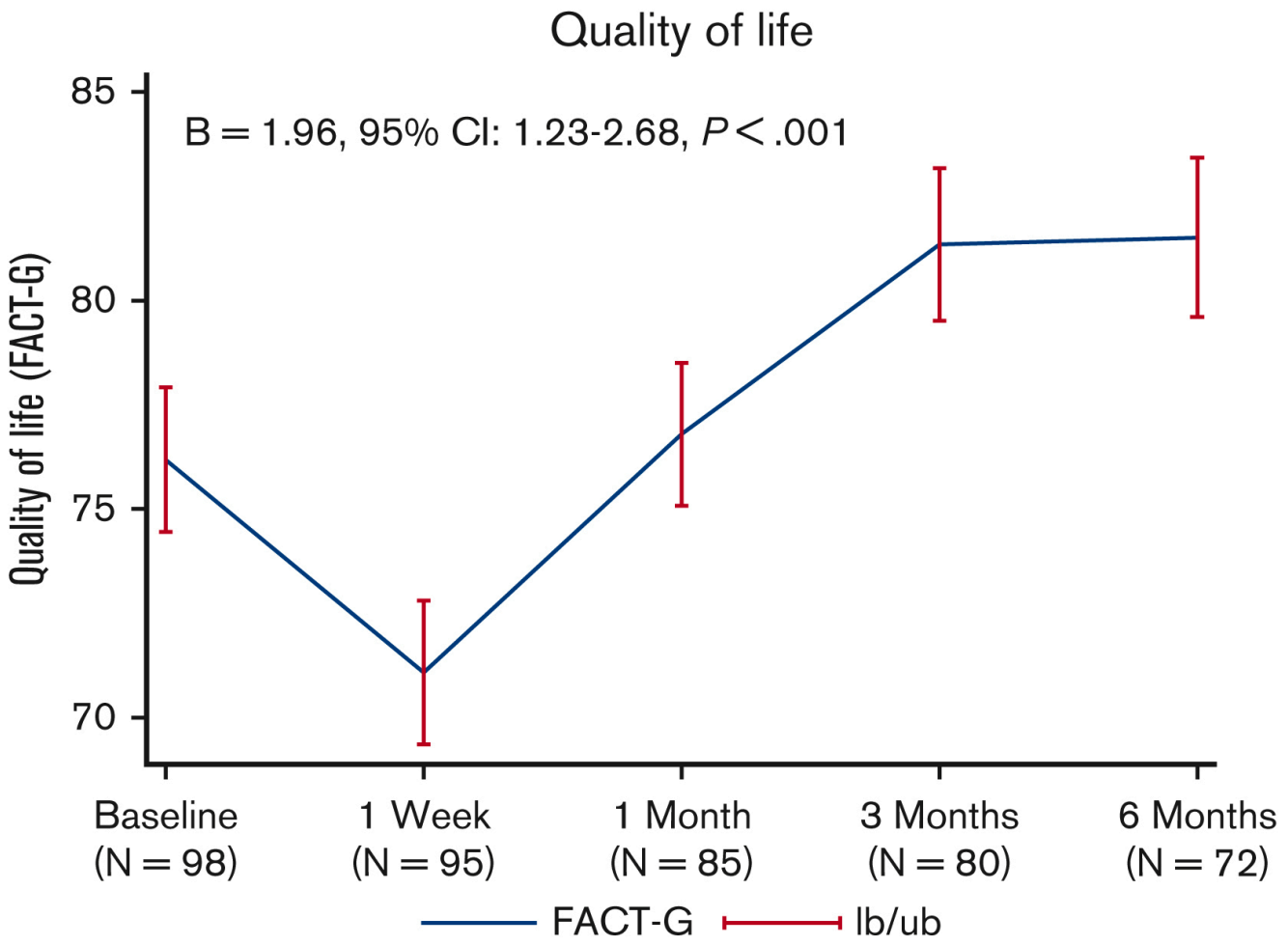
Jacobsen, J Palliat Med 2018; Lai-Kwon, J Cancer Survivorship 2021

Early Recovery After CAR-T

- Patients typically followed closely at CAR-T center until day 30-60
- Close monitoring for CRS and neurotoxicity during the first 30 days
- Often living away from home during first 30 days after CAR-T
- Residual physical and functional limitations early after treatment
- Fatigue common and persistent up to 6 months post-CAR-T
- Risk of infections after treatment (viral is biggest risk)

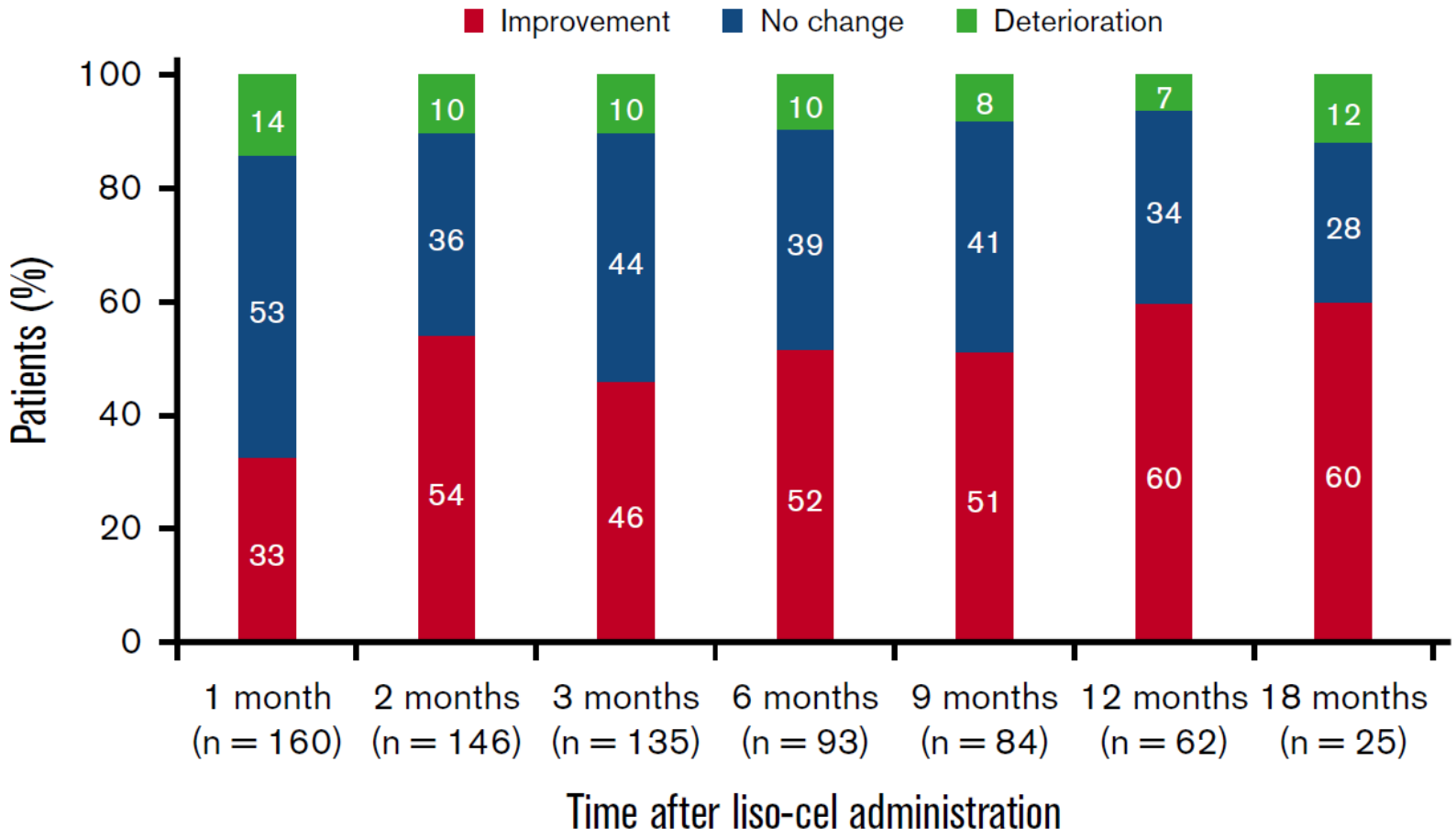
Quality of Life (QOL) During and After CAR-T

- QOL measured over time (higher is better)
- On average improving by 3-6 months after CAR-T and similar to US population average
- No factors were associated with negative QOL trajectory



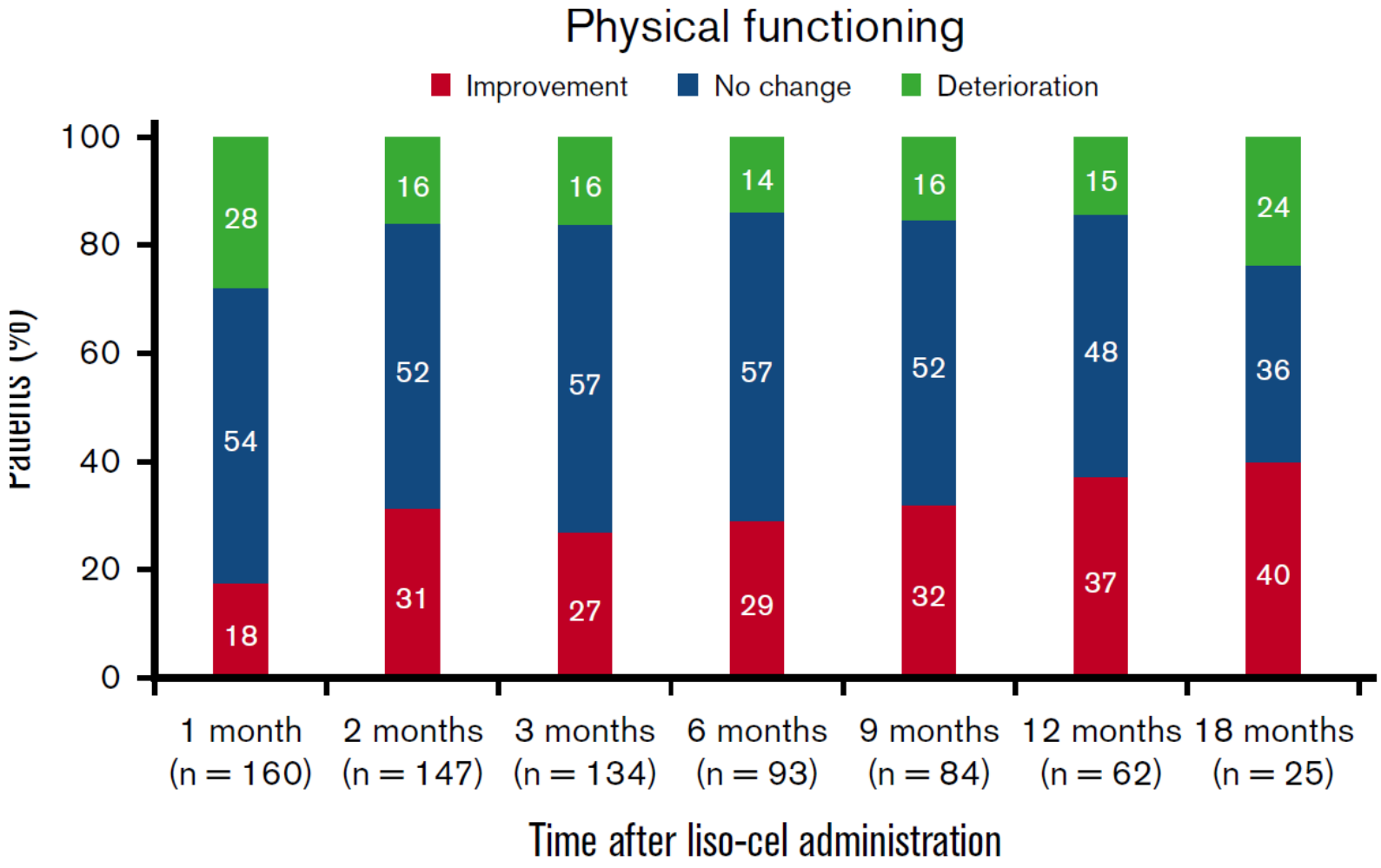
Johnson, et al. Blood Advances 2023.

Early Recovery after CAR-T for Lymphoma



Patrick DL, et al. Blood Advances 2021

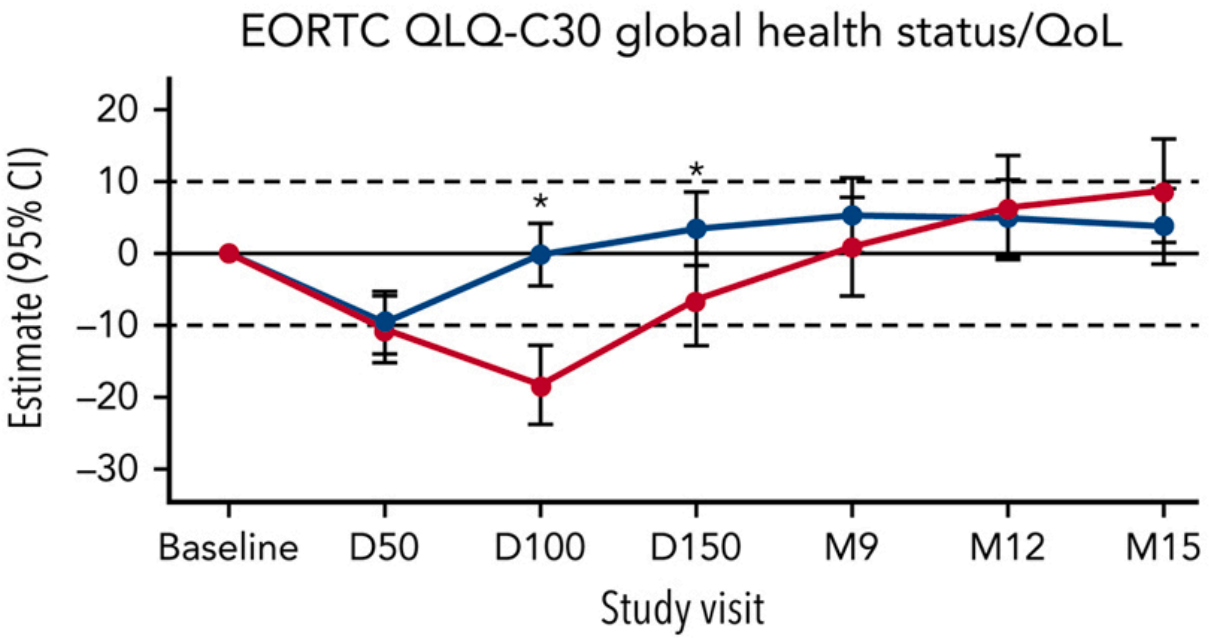
Early Recovery after CAR-T for Lymphoma



Patrick DL, et al. Blood Advances 2021

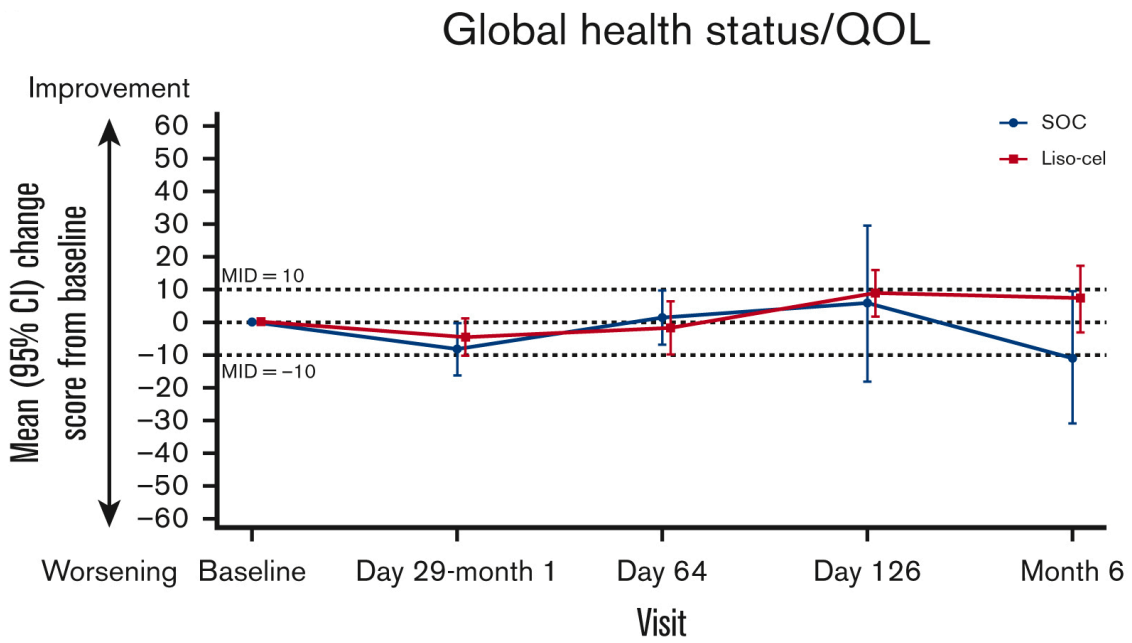
Quality of Life with CAR-T Compared to Chemotherapy in Lymphoma

CAR-T in Blue



Axi-cel	165	163	146	110	88	79	67
SOC	130	125	62	56	40	33	26

CAR-T in Red

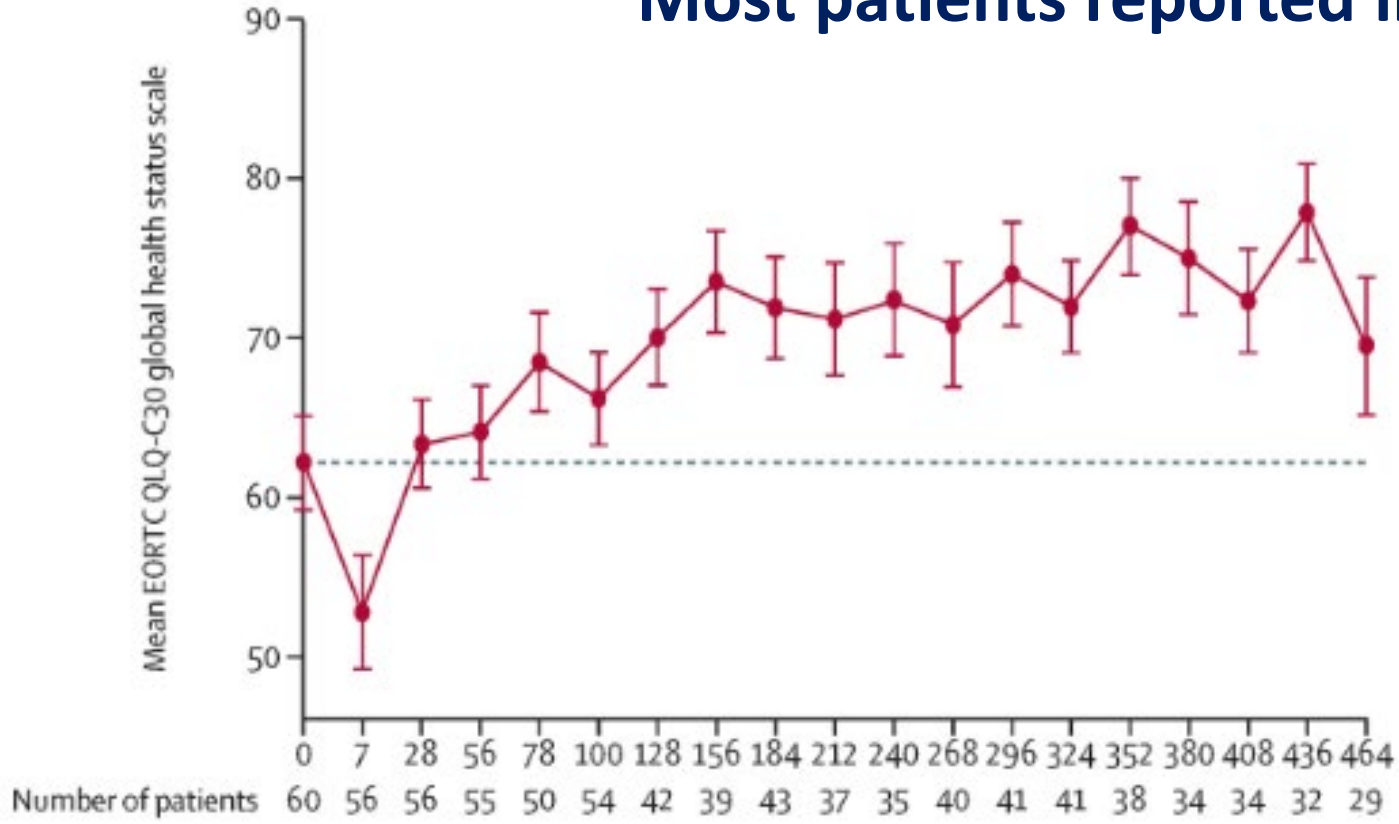


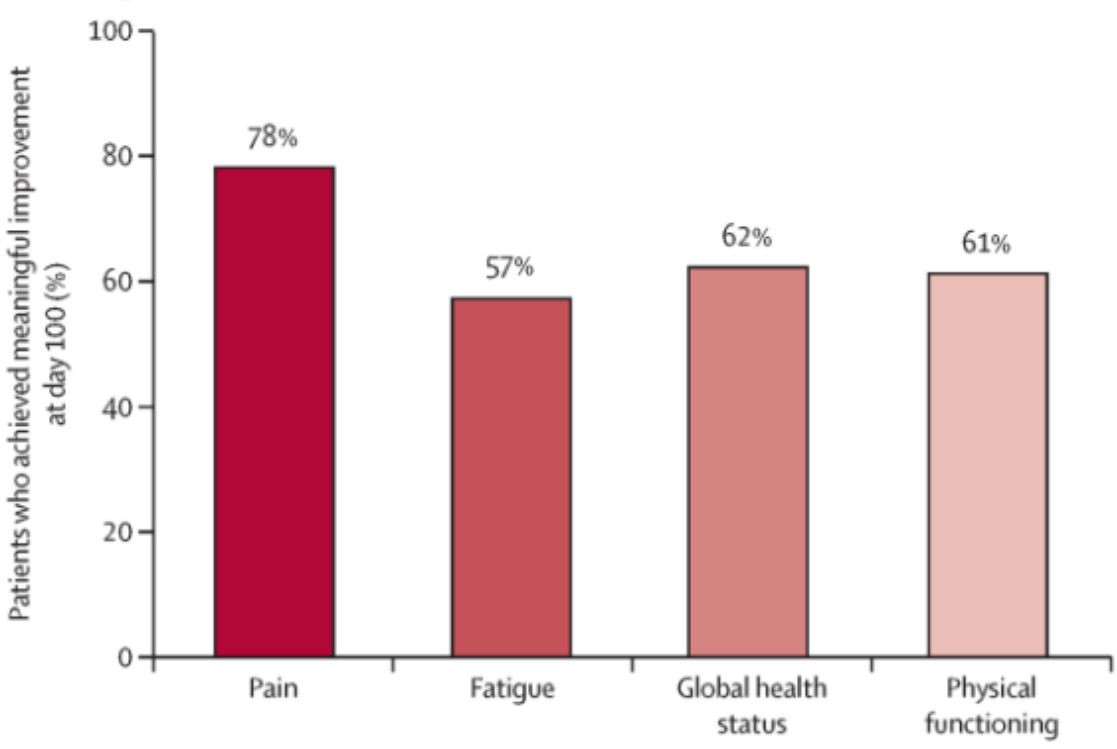
No. of patients					
SOC	43	39	36	10	7
Liso-cel	47	41	37	26	17

Elsawy et al. Blood 2022. Abramson, et al. Blood 2022.

Early Recovery After CAR-T for Myeloma

Most patients reported improvement at day 100

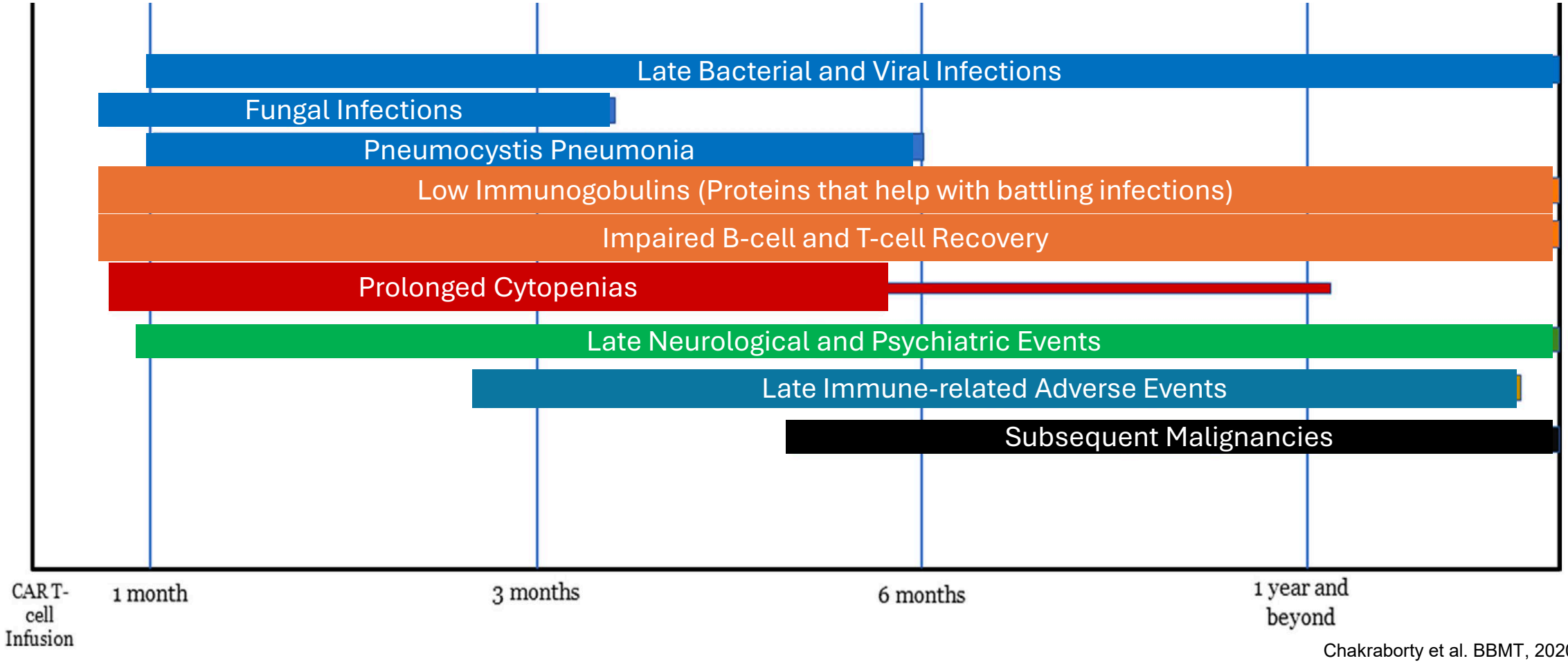




Martin, et al. Lancet Haematology 2022

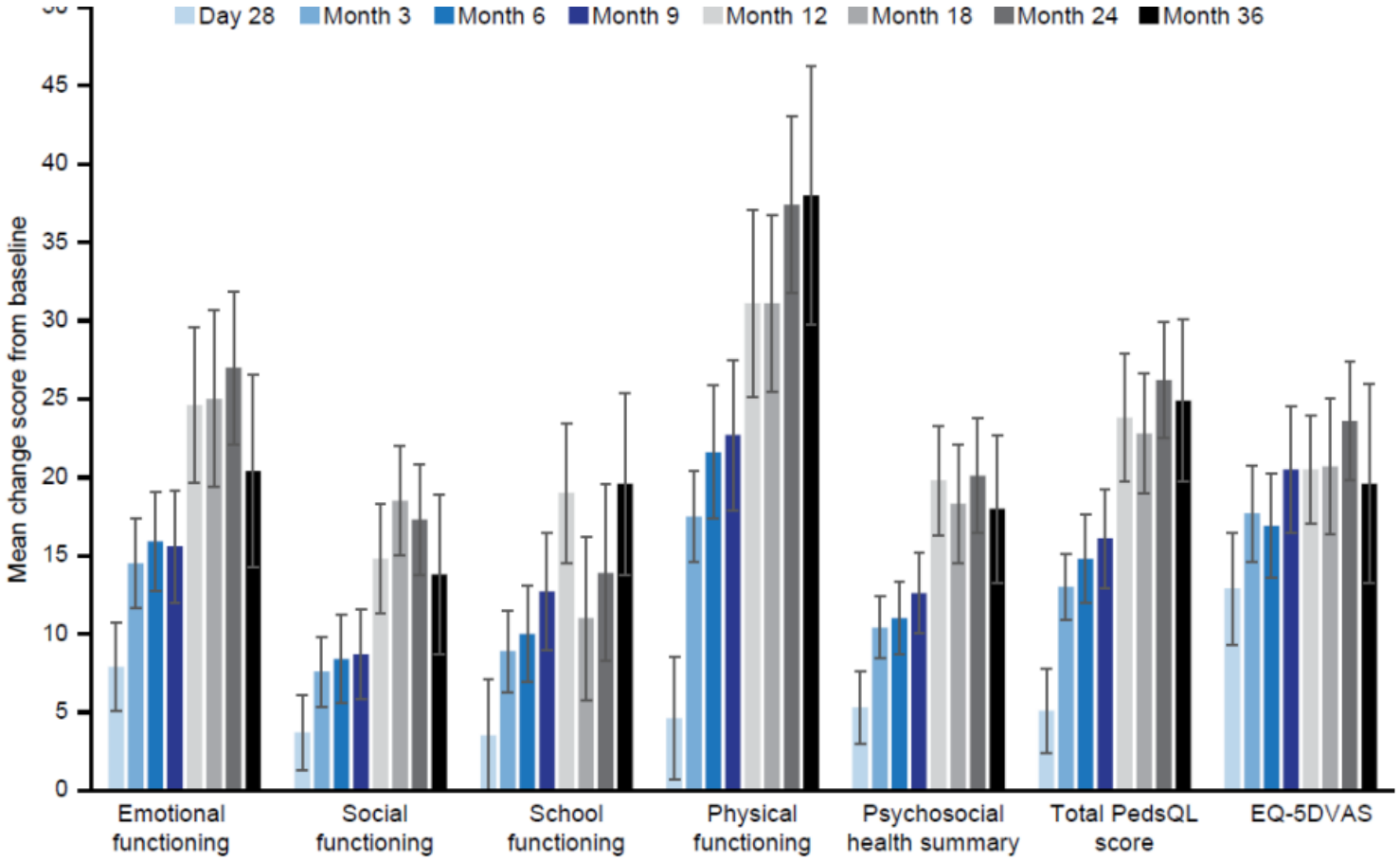
Survivorship after CAR-T

Survivorship Concerns



Chakraborty et al. BBMT, 2020

Long Term Quality of Life After CAR-T for Leukemia in Pediatrics and Young Adults



Laetsch, et al. Journal of Clinical Oncology 2023

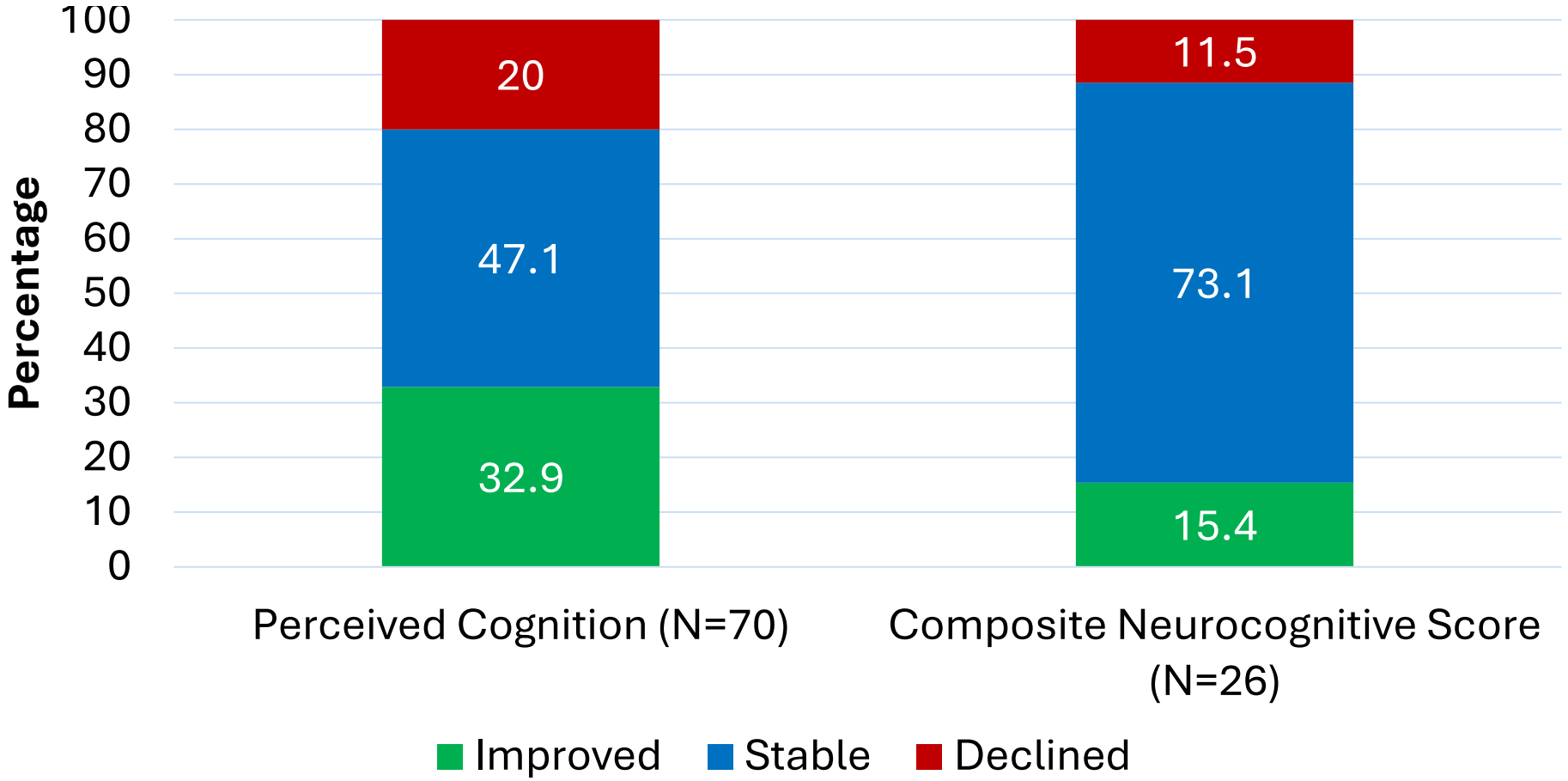
Survivorship Concerns

- Compared to the general population, CAR-T survivors at 1-5 years post-CAR-T were *not* different in:
  - Quality of life scores
  - Physical health
  - Mental health
- 37.5% reported cognitive difficulties

Ruark et al. Transplant Cell Ther, 2019

Neurocognitive Outcomes 6 Months After CAR-T

- No difference in average scores 6 months after CAR-T compared to baseline
- No response to CAR-T was associated with worse neurocognitive outcomes



Barata et al. [Unpublished]

Movement and Neurocognitive Treatment-Emergent Adverse Events (MNTs)

- Paralysis of cranial nerves or syndrome that resembles Parkinson's disease with tremors, trouble with movement, memory difficulties
- Occurs with CAR-T cell therapies, primarily targeting BCMA, which is used in multiple myeloma, most commonly with cilta-cel
- Poorly understood, but often occurs more than 4 weeks after infusion
- Risk factors appeared to be high tumor burden, higher grade CRS, presence of neurotoxicity, high levels of persistent CAR-T cells
- In one study occurred in 5% of cilta-cel patients
- Treatment is evolving, usually involves steroids or cyclophosphamide
- More aggressive bridging therapy strategies and CRS/neurotoxicity treatment may reduce the risk

Cohen et al. 2022

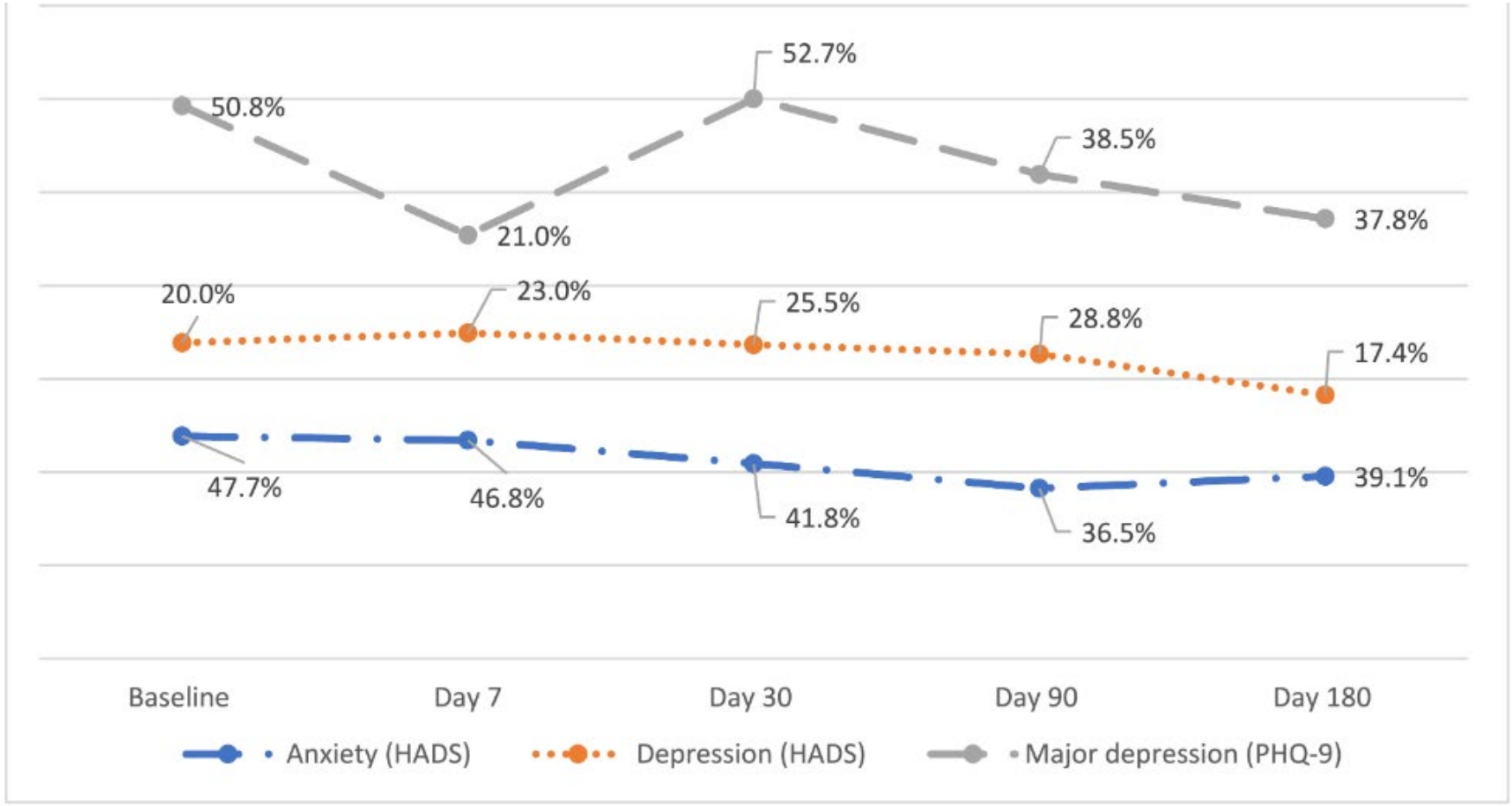
Second Cancers after CAR-T

- 25/724 patients developed second cancers after CAR-T with a median follow up of 15 months (3.4%)
  - 13 patients had myelodysplastic syndrome or acute leukemia (1.8%)
  - 1 patient had a T-cell lymphoma (0.1%)
  - 11 patients had solid tumor malignancies (1.5%)

Effect on Caregivers

- Caregivers provide majority of care for CAR-T recipients
- Caregivers monitor for toxicities early in the recovery period
- Caregivers have a stressful job
- Chronic caregiving especially in the context of CAR-T
- Immense caregiving burden
- Impact on relationships
- Impact on caregiver health
- Financial burden is immense

Effect on Caregivers



Barata et al. Transplant Cell Ther. 2024.

Conclusions

- Generally, quality of life and symptom burden improve over time after CAR-T across blood cancers
- Quality of life decreases by two weeks after CAR-T but improves on average by 3-6 months after CAR-T
- CAR-T survivors have quality of life similar to the general population
- Physical and psychological symptoms improve, though for a subset of patients can persist
- Cognitive outcomes long-term appear good based on research to date
- Caregivers of patients receiving CAR-T experience significant psychological symptoms

Questions?

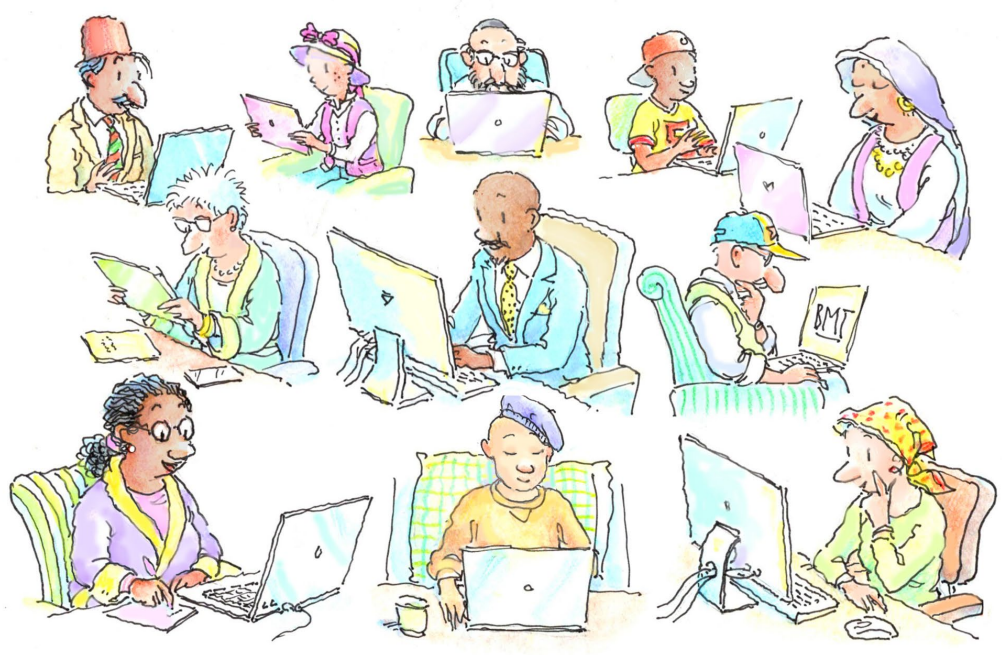
Sarah Meredith
High Risk Myeloma
CAR T May 2022

P. Connor Johnson MD
Massachusetts General Hospital

Paul Gerhardt
Follicular Lymphoma
CAR T May 2021

Many thanks to Bristol Myers Squibb whose support helped make this presentation possible.

Let Us Know How We Can Help You!



Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

Find us on:

facebook.com/bmtinfonet

Instagram.com/bmtinfonet

twitter.com/BMTInfoNet

Many thanks to Bristol Myers Squibb whose support helped make this presentation possible.

BMTinfonet.org 30 YEARS EMPOWERING PATIENTS