The landmark US Food and Drug Administration approvals last year of tisagenlecleucel and axicabtagene ciloleucel – the first two chimeric antigen receptor (CAR) T-cell therapies for cancer – signified a new era of therapeutic possibilities (p. e124). CAR T-cells are a type of adoptive cell therapy or immunotherapy in which a patient’s immune cells are genetically engineered to target a tumor-associated antigen (in the case of these first two approvals, that target is CD19). In August, tisagenlecleucel got the green light for the treatment of B-cell precursor acute lymphoblastic leukemia in patients up to age 25 years, and in the fall, axicabtagene ciloleucel was approved for the treatment of refractory, aggressive B-cell non-Hodgkin lymphoma. The earlier this year, the agency also approved tisagenlecleucel for adult patients with relapsed or refractory large B-cell lymphoma. As Carl June, MD, a pioneer in CAR T-cell research notes in an interview on page e175, the next approval likely will be for multiple myeloma.

But while the science and the potential of these therapies are exciting, the impact of their cost and toxicities on patients tempers some of the enthusiasm. The Centers of Medicare & Medicaid Services is working on a final rule on payment for the inpatient administration of the two therapies for fiscal year 2019 and is considering the creation of a new Medicare Severity-Diagnosis Related Group code for procedures involving the use of CAR T-cell therapies (p. e177). Walid F Gellad, MD, of the Center for Pharmaceutical Policy and Prescribing at the University of Pittsburgh, has said that some estimates for the cost of these therapies as high as $1.5 million per patient, and there is particular concern for the older adults who make up the Medicare population. These high costs would affect access to the therapy for many patients, irrespective of age, but one encouraging development on this front would be the development of lower-priced, off-the-shelf, third-party products. Another unknown with CAR T-cell therapies is the extent of side effects in real-world patients compared with those in trials, and what the long-term posttherapy recurrence rates would be.

In addition to highlighting CAR T-cell therapies in this issue, on page e167, Jane de Lartigue takes a look at tumor heterogeneity and the challenges it presents in the ongoing quest for effective cancer treatments. Dr de Lartigue describes the two key models used to explain how tumors develop – the clonal evolution model and the cancer stem cell model. She argues that although evidence suggests the models are not mutually exclusive and contribute to heterogeneity differently in different tumor types, heterogeneity and evolution, fueled by genomic alterations, are “intricately intertwined” in the development of cancer.

With cancer therapies come side effects, psychosocial effects, and sometimes challenges with posttreatment mobility, activities of daily living, and even self-care. Three articles in this issue deal with those posttreatment issues. On page e130, Kundu and colleagues report on a prospective study in which they evaluated physical and psychosocial functioning after diagnosis of prostate cancer and the factors associated with treatment satisfaction after treatment. They found that despite declines in erectile function and sexual domains, treatment satisfaction was more closely related to emotional, psychosocial, and nonsexual effects, underscoring the importance of assessing health-related quality-of-life outcomes beyond physical functioning. Forrest and colleagues (p. e138) set out to report outcomes of patients who received radiation therapy while on an inpatient rehabilitation facility and found that comprehensive care that includes radiation and rehabilitation at the inpatient rehabilitation facility level benefits appropriately selected patients. And on page e145, Ibrahim and colleagues tracked the effectiveness of a 12-week exercise program on long-term levels of upper-limb pain in young survivors of breast cancer and found that although there was some transient improvement in shoulder pain, it did not translate into long-term benefits.

Our usual line-up of Case Reports on clinical challenges in the practice setting includes the case of a child with carcinoma of the colon (p. e152); two separate reports on patients with therapy-related skin reactions, one with radiation dermatitis (p.e156), the other with a reaction to a checkpoint inhibitor (p. e159); and a patient with recurrence of a small gastric gastrointestinal stromal tumor with high mitotic index (p. e163).