In December 2017, the Boston radio station WBUR chronicled the case of the first patient at Massachusetts General Hospital to receive axicabtagene ciloleucel (Yescarta, Gilead) outside a clinical trial. The chimeric antigen receptor T cells (CAR-Ts) were made from 71-year-old Barbara Kearney's own T cells, which after genetic modification ex vivo were turned on to target the CD19 receptor. CD19 is a commonly expressed surface antigen on B cells, including those of Ms. Kearney's non-Hodgkin's lymphoma, and also inhabits the surface of some other normal cells.1

In a trial involving 101 patients with non-Hodgkin's lymphoma, axicabtagene ciloleucel produced complete remission in 51, which led to its approval by the Food and Drug Administration (FDA). Tisagenlecleucel (Kymriah, Novartis), another anti-CD19 CAR-T therapy, led to complete responses in 22 of 69 patients (32%). Juno Therapeutics also has a development program for anti-CD19 CAR-T therapies. (I have been involved in various ways with all three manufacturers.)

The two approved CAR-T therapies have boxed warnings regarding serious side effects, and each costs about $400,000. Ancillary costs include initial leukapheresis and inpatient stays that may be necessitated by frequent treatment complications, which may result in administration of tocilizumab (up to four doses at $2,500 per dose). Hernandez and colleagues estimate that these ancillary costs would average around $33,000 per patient; media reports suggest a figure 10 times as high.2

The small number of studied patients and the high price of the treatment and ancillary costs led United Healthcare, a provider of Medicare Advantage plans, to request that the Centers for Medicare and Medicaid Services (CMS) perform a national coverage analysis (NCA) of CAR-T therapy. United argued that implementing a single coverage policy for CAR-T therapy across Medicare would level the financial playing field for competing plans and ensure equal access. NCAs do usually result in uniform coverage across Medicare; without them, coverage often varies among regions and plans.

Under the 1965 law that created Medicare, the program must cover services that are “reasonable and necessary” for the treatment of illness. CMS interprets this phrase as requiring coverage of services that provide a net benefit. The agency does not consider
a therapy’s price, and the part of CMS that determines coverage is separate from the part that determines payment rates. Yet in recent years, as the costs of treatments have increased, CMS has adopted an approach to coverage determinations that takes a stricter view of the evidence.⁴

The agency may find the trial data sufficient to conclude that CAR-T therapy provides a net benefit for Medicare patients. But such a conclusion would be based on observations from only a handful of patients 65 years of age or older (and thus age-eligible for Medicare). If CMS reaches this conclusion, it need not simply say yes to coverage. It could limit coverage to patients enrolled in a clinical trial. If CMS can drive price competition, for instance, or it could use the Coverage with Evidence Development (CED) designation, which can either include a requirement that further outcome data be collected in a registry or limit coverage to patients enrolled in clinical trials. In either case, CED aims to buttress the evidence relevant to the “reasonable and necessary” question.

In tandem, the Center for Medicare and Medicaid Innovation at CMS could design a payment approach for CAR-T therapy that promotes competition based on price — an improvement over the current system, which includes such therapy in Part B drug reimbursement and provides doctors and hospitals with larger profits when the treatment costs more.

To decide among this array of options, CMS will have to determine whether it has adequate confidence on two points regarding the various CAR-T therapies: whether their net benefits are similar and whether the ancillary services have similar costs. The table outlines alternative approaches to coverage for CAR-T therapies based on the answers to these questions with reference to the overlapping indication for the two approved agents — recurrent or refractory B-cell lymphoma. This indication is more prevalent than the additional indication for tisagenlecleucel — pediatric and young adult acute lymphocytic leukemia.

If CMS is adequately confident that the net benefit is similar, it could promote price competition, but how this could be done would depend on the ancillary health care costs associated with use of the treatments. Concluding that the ancillary costs are likely to be similar would let the agency focus solely on price competition between the CAR-T therapies; if it lacks confidence on that question, CMS could promote price competition in a manner that incorporates both the cost of the CAR-T therapy and the ancillary costs.

But CMS may also lack confidence that the various therapies have similar net benefits, in which case it could limit coverage to patients enrolled in a clinical trial. A randomized trial comparing the CAR-T therapies, and involving 3450 patients, would have power to confirm similar benefit with a ±5% margin if the response rate were 50%. About 7500 patients per year would be expected to have the relevant condition, and the majority of them would be Medicare-eligible.⁵ It would make sense to examine quality of life, resulting financial difficulties for patients, and variation in efficacy across patient subgroups as outcomes in such a study, and data on ancillary costs should also be gathered if CMS cannot conclude that the costs are similar for different therapies.

CMS can drive price competition on CAR-T therapy alone by soliciting bids from the competing manufacturers. The agency has engaged directly in such competitive bidding for durable medical equipment and has engaged a pri-
vate contractor to do so for Part B drugs under the Competitive Acquisition Program (CAP). CAP was recently highlighted in President Donald Trump’s “blueprint to lower drug prices.” Or CMS could consolidate billing for comparable CAR-T therapies into a single code, which would lead to price competition among manufacturers, since reimbursement to doctors and hospitals is based on a weighted average of sales of all drugs incorporated into the billing code. Thus, the lowest-priced CAR-T therapy at a given time would provide a larger profit to the prescriber, and manufacturers would strive to undercut one another. Deploying consolidated billing codes to drive price competition is a strategy that was recently highlighted by the Medicare Payment Advisory Commission (MEDPAC).5

Ancillary costs can be incorporated under case-rate (bundled) lump-sum payment, which forces the physician or hospital to take financial responsibility for the total cost of using the therapy, including management of its complications. The provider’s profits increase if the total cost of care is less than the lump-sum amount, which creates an incentive to select the therapy associated with lower total costs. These choices, in turn, drive manufacturers to lower their prices. Gain sharing is similar to case-rate payment but is implemented after the fact, and typically only a fraction of the savings is returned when costs fall below a benchmark. Then again, only a fraction, or sometimes none, of the losses are borne by the provider when the reverse occurs.

CAR-T therapies have broken new ground on many fronts — they have shown efficacy in patients who previously had few options, but they cost multiple times what any previously approved cancer therapy costs. Their rapid approval based on small, uncontrolled studies reflects their promise. But they are no panacea. Ms. Kearney died a few weeks after receiving her dose of the CAR-T therapy that cost nearly $400,000, and she endured an extended hospital and ICU stay along the way. She told WBUR reporter Richard Knox that she knew death was a possible outcome, and she was grateful for the chance to receive a possibly effective treatment — a reminder of what’s at stake for Medicare patients when CMS considers CAR-T therapy coverage. If Medicare chooses to cover this therapy, it should think carefully about how to do it.

Disclosure forms provided by the author are available at NEJM.org.

From the Center for Health Policy and Outcomes, Memorial Sloan Kettering Cancer Center, New York.

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