Doctors Work on When to Stop Cancer Immunotherapy

**By Brianna Abbott and Jared S. Hopkins**

Immune-boosting rugs have revolutionized cancer care. Now doctors are experimenting with cutting them off.

Immunotherapies unleash the immune system on tumors. They have extended the lives of people with melanoma and lung and bladder cancers. They have also been a boon for drugmakers, generating global sales of $44 billion in 2022, according to Leerink partners analysts.

But some patients are getting more of the drugs than they need, exposing them to side effects and costs they could avoid without risking their cancer’s recurring. Preliminary research suggests taking the drugs at the lower dose or for a shorter period could be sufficient, but drugmakers haven’t funded the studies needed to confirm said it balances effectiveness and safety in setting the recommended dose the findings.

“We don’t know when to stop,” said Dr. Jedd Wolchok, an oncologist focused on melanoma at Weill Cornell Medicine in New York.

Doctors are already doing less chemotherapy, radiation, and surgery for lower risk cancers. Researchers at a conference in San Antonio this month showed some low-risk breast-cancer patients could safely skip radiation or get follow-up screening less often.

Recalibrating care toward less treatment is a fraught undertaking. Drug companies won’t fund studies exploring whether patients can do as well with less of their products, doctors said. Some doctors and patients worry about pulling back before exhausting their best chance to beat the disease.

“There was this dogma that more is better,” said Dr. Mark Ratain, an oncologist at the University of Chicago.

He is trying to recruit cancer patients to study whether they could do as well with less of Merck’s Keytruda or Bristol-Myers Squibb’s Opdivo, so-called immune checkpoint inhibitors. After three years, he has found just 60 of the 260 patients he wants, and most medical centers have declined to join the trial, “It was going to be difficult to convince people,” he said. Merck said it balances effectiveness and safety in setting the recommended doses for its cancer drugs. It said it is focused on how approved drugs could help patients in combination with other treatments rather than re-evaluating its original dosing.

Bristol said standard dosing for Opdivo is supported by robust evidence that it is effective and tolerable. One Bristol study found that lung-cancer patients who got Opdivo infusions for two years rather than one experience better outcomes.

Lodi Vercelli, a 67-year-old from Wilmington, Ill., joined Ratain’s study when his esophageal cancer came back six months ago. “You hear some stories that some people have had some pretty nasty side effects from immunotherapy,” Vercelli said. “Maybe half a dose was the way to start this thing.”

He said he hasn’t experienced side effects after five months of treatment. His most recent scans suggest the drug is working.

People taking immunotherapies often experience itchy skin and rash, diarrhea and joint pain. Rare side effects including thyroid problems or pancreatitis can occur well into treatment.

“Every therapy that we do in a double-edged sword,” said Dr. Yuan Yuan, an oncologist focused on breast cancer at Cedars-Sinai Cancer in Los Angeles.

Many patients who stop taking the drugs before finishing the standard one-to-tow years of treatment because of side effects still do well, preliminary research shows. A report this month in the journal Cancer Research Communications found that most metastatic colon cancer patients who responded well to their initial treatment didn’t experience a worsening of their disease nearly two years after discontinuing the drug.

“All patients probably don’t need a long duration of therapy to have durable benefits,’’ said Dr. Geoffrey Gibney, a melanoma doctor at the Georgetown Lombardi Comprehensive Cancer Center.

He is testing whether advanced melanoma patients can discontinue Keytruda, Opdivo or Bristol’s Opdualag if they appear disease-free after one year of treatment. About 35 of the 150 patients, he is seeking have joined so far.

Stopping treatment earlier would also save patients from continuing to pay for the drugs. Keytruda has a list price of $11,115 for a dose given every three weeks, while Opdivo has a list price of $14,389 for a dose given every four weeks.

Bristol said the final price for Opdivo depends of factors including how long it is administered and the combination of drugs a patient receives. Merck declined to comment on Keytruda’s cost.

At Tata Memorial Hospital in Mumbai, most patients eligible for immunotherapy couldn’t afford it, said Dr. Kumar Prabhash. An oncologist, Prabhash found that head-and-neck cancer patients experience a significant survival benefit with chemotherapy plus Opdivo at 6% of the dose used in the U.S., compared with patients who got chemotherapy alone.