Does Timing of Immunotherapy Really Matter?

Medical journal retracts a study that claimed to show receiving cancer treatment early in the day led to better outcomes.

July 2, 2026 By Liz Highleyman

Earlier this year, researchers published study results suggesting that lung cancer patients who were treated with immunotherapy before 3 p.m. had more cancer-fighting T cells and lived longer than those treated later in the day. But further analysis cast doubt on the findings, and the report has been retracted. This can be seen as good news for cancer patients and busy oncology practices, which now have one less thing to worry about.

The timing of treatment to maximize effectiveness and minimize toxicity is gaining interest in oncology and other medical fields, but it is not yet well understood. The idea is to take advantage of circadian rhythms, or variations in biological processes over the course of the day. Research in animals and humans has shown that the immune response waxes and wanes at different times of day.

Studies of treatment timing have yielded conflicting results. Most have been retrospective, meaning they used medical records to look back at outcomes among patients enrolled in trials with other objectives.

For example, Zhe Huang, MD, of Hunan Cancer Hospital in China, and colleagues published a study last year showing a survival benefit for small-cell lung cancer patients who received immunotherapy before mid-afternoon. A morning advantage was also seen in a study of patients with metastatic kidney cancer treated with checkpoint inhibitors at City of Hope Cancer Center in California. Another study found that people with non-Hodgkin lymphoma who received infusions of CAR-T therapy earlier in the day had longer progression-free survival.

Timing may work differently for chemotherapy, which directly kills cancer cells rather than strengthening the immune response. A 2023 study of lymphoma patients found that women who received chemotherapy in the morning had more adverse events, more treatment delays or dose reductions and poorer outcomes than those treated in the afternoon, though the same association was not observed for men.

Retrospective analysis can introduce bias because people who receive treatment earlier in the day

may be differ from those treated earlier—for example, they may have different types of jobs, potentially reflecting varying education and income levels, or may live closer to infusion centers. In contrast, the retracted study—also by Huang's team—was a prospective Phase III randomized clinical trial specifically designed to compare outcomes among people receiving treatment at different times of the day.

The LungTIME-C01 trial (NCT05549037) enrolled 210 people at a single center in China who had previously untreated Stage IIIC to IV non-small-cell lung cancer without driver mutations that would make them eligible for targeted therapies. They were randomly assigned to receive their first four cycles of PD-1 checkpoint inhibitor infusions before or after 3 p.m. Most were treated with sintilimab (Tyvyt), which is approved in China but not the United States, while the rest received pembrolizumab (Keytruda.)

According to the February report in Nature Medicine, patients treated in the morning or early afternoon had improved progression-free and overall survival. After about two years of follow-up, those in the early group had a median progression-free survival time of 11.3 months, compared with 5.7 months for the late group. The median overall survival time also doubled in the early group: 28.0 months versus 16.8 months. In both comparisons, disease progression or death fell by about 60% with early treatment. In addition, people treated earlier in the day saw an increase in circulating CD8 T cells—the immune system's main cancer fighters—while those in the late treatment group showed a decline.

A few weeks after publication, the journal editors announced that they were looking into concerns expressed about the study's protocol and findings. After a four-month investigation, they decided to retract the report, stating that they "no longer have confidence in the integrity of the results."

In particular, the editors noted concerns about discrepancies between the trial protocol recorded in advance on ClinicalTrials.gov and the published version as well as differences between the original protocol in Chinese and the translation provided for peer review and publication. They pointed to some major changes to the study design, sample size, eligibility criteria and endpoints that were made after the trial was already underway. What's more, some of the safety results raised questions, such as similar rates of adverse events despite differences in efficacy and the fact that no one dropped out of the trial due to side effects.

The trial's senior author, Yongchang Zhang, MD, of Hunan Cancer Hospital, said in a statement that an internal review had "confirmed that part of the study execution and manuscript preparation might not reach the standards for publication in a high-impact journal," The New York Times reported.

Upon publication, the study made waves, with some experts suggesting it would lead to major changes in clinical practice. Others, however, were more skeptical that treatment timing could make such a big difference. Checkpoint inhibitor monoclonal antibodies last for weeks in the body—and modified CAR-T cells can persist for several years—so what time of day they are administered might not matter.

Toni Choueiri, MD, of Dana-Farber Cancer Institute, who contributed to the post publication review, told the Times that the study findings were “too good to be true.” But if they were true, it would not necessarily be good news.

Trying to schedule most patients for treatment early in the day would be logistically difficult for doctor’s offices, infusion centers and hospitals. “In institutions where treatment flows are tightly choreographed for efficiency, redistributing resources to ensure a consistent morning window for immunotherapy may require re-engineering schedules, additional staffing or extended pharmacy hours—all without additional reimbursement,” Gilberto Lopes, MD, of the University of Miami’s Sylvester Comprehensive Cancer Center, wrote in an opinion piece for ASCO Connection.

What’s more, variable treatment efficacy based on the time of day would also raise concerns about equity, as people with inflexible work schedules, transportation limitations or childcare needs might not be able to schedule their treatment in the morning. The best news would be that treatment is equally effective no matter when it’s given.

Click here for more news about cancer treatment.
