
FAQ: What is Neoadjuvant Therapy and Why Would We Want to Give it?

The cornerstone of treatment of an earlier stage cancer is a local therapy such as surgery or radiation, which is meant to remove or destroy the cancer that is limited to a specific area. We know, however, that people who have undergone complete resection or what should be complete destruction of a tumor by radiation will too often have their cancer return, sometimes near the area where it first appeared, but often in a distant location. When we see the cancer recur in a distant site, we can presume that this was mediated by “micrometastatic” disease, circulating tumor cells that were too small to be seen on any scans or by a surgeon directly at the time of surgery, but which must have remained in the body after a good local treatment removed or destroyed all evidence of visible disease. In order to combat this risk and try to treat potential micrometastatic disease, we often give systemic therapy before and/or after the local therapy. A particularly common approach is to follow surgery with chemotherapy, which is called adjuvant therapy, with adjuvant meaning “helper”. Systemic therapy before surgery or possibly before radiation is typically termed neoadjuvant therapy, and there are a few reasons why we might prefer to give systemic therapy at the earliest opportunity, rather than having it follow the potentially curative local therapy.

First, we might be concerned about the potential for cancer to spread during the time between the initial diagnosis and the time when a patient is ready to start systemic therapy after recovering from surgery. Neoadjuvant therapy provides an opportunity to treat both the visible and potential invisible cancer at the earliest time point.

Second, it is possible to assess the response to an initial systemic therapy in order to get a sense of whether the treatment worked well, and this can help inform a decision about whether any further systemic therapy, whether the same or a different kind, would be beneficial to give after surgery or radiation, in the adjuvant setting. If a patient undergoes surgery, it is even possible to see at the tissue and molecular level how the preoperative therapy affected the tumor tissue. This sometimes leads to “window of opportunity” trials in which a novel therapy is given prior to planned surgery in order to assess how cancer responds, both in terms of imaging after the preoperative therapy and in effects observed directly on the tumor tissue under a microscope.

Third, it is sometimes possible to shrink a cancer with neoadjuvant therapy that makes it possible for a patient to undergo a less extensive surgery (or smaller radiation field), or to undergo a surgery for which he or she was a marginal candidate because of the large size of the cancer initially.

Finally, the local therapy itself, particularly surgery, can often be very challenging and pose risks of a difficult recovery. If we know that we want to give a combination of systemic therapy and local therapy, it is most reliable to give the systemic therapy first, after which very few patients will miss an opportunity for the local therapy, in contrast with starting with the



challenging surgery and then having a significant subset of patients not recover well enough to pursue the tended systemic therapy.

The leading concern about giving systemic therapy first in patients who are candidates for a curative local therapy right at the time of diagnosis is that a small minority of patients may demonstrate progression systemic therapy and demonstrate a larger tumor or metastatic disease after neoadjuvant therapy. While this would translate to having a lower or no chance for cure, such patients would be extremely unlikely to be cured with immediate surgery as well, likely demonstrating the same progression before even recovering from their local therapy.

Neoadjuvant therapy is employed for many cancers, including lung, breast, colorectal, and several others, as an optimal strategy for many patients.

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